

Supporting Information

Biphasic Electrochemical Peptide Synthesis

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1. Additional Figures

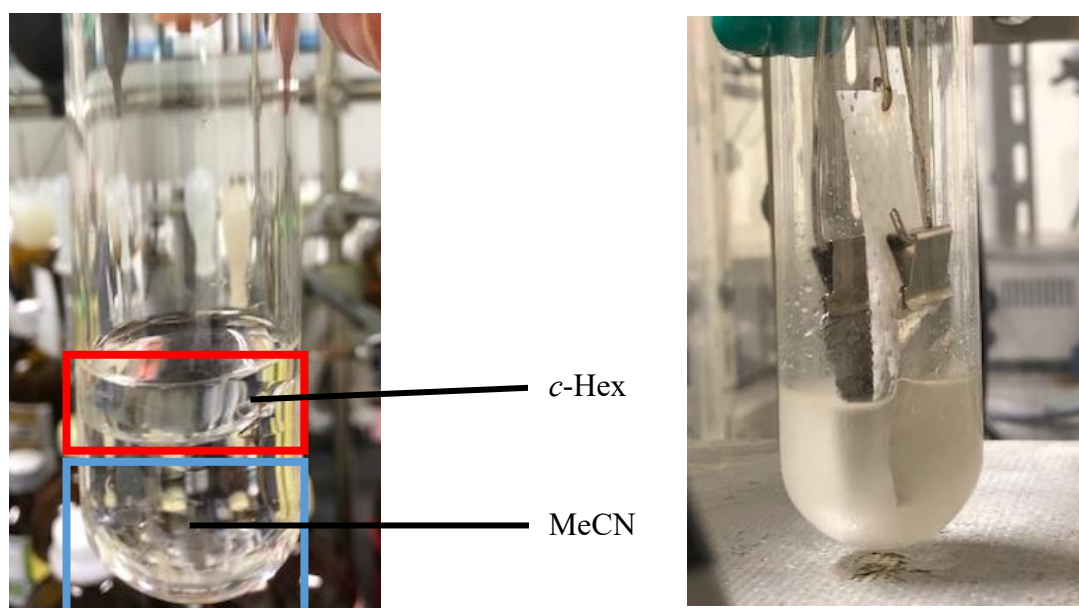
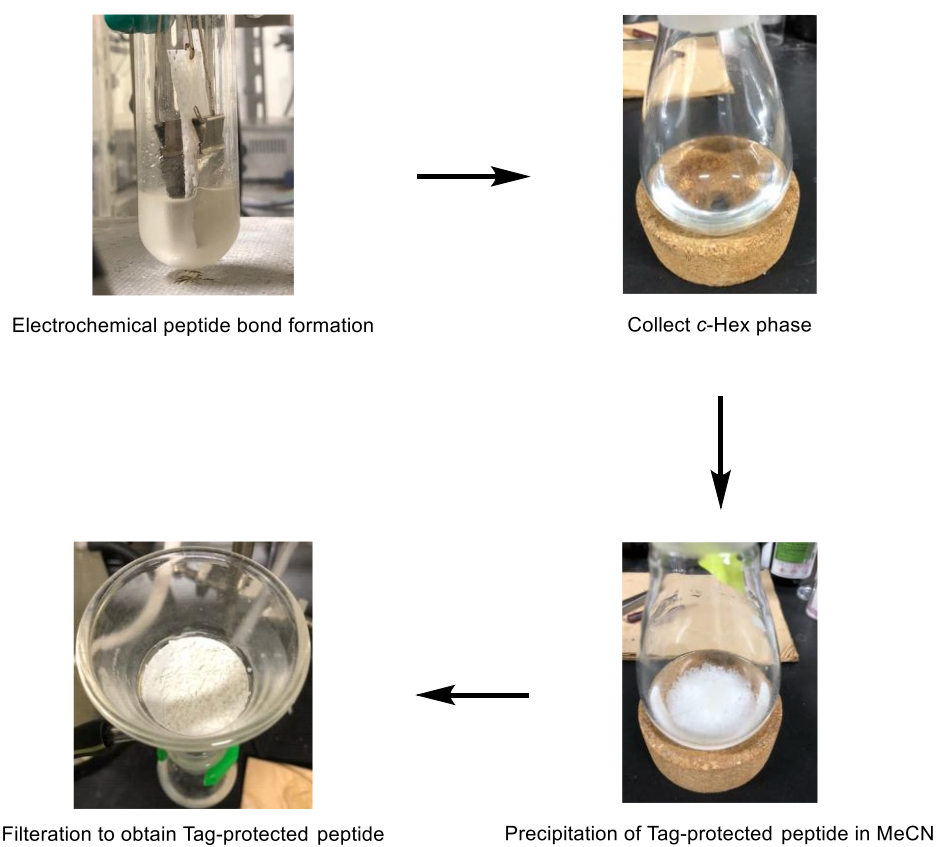


Figure S1. Biphasic Reaction System; Before electrolysis (left), and during electrolysis (right).



Scheme S1. The Process of Biphasic Electrochemical Peptide Synthesis.

2. Experimental Section

2.1 General Information

All reagents and solvents were purchased from commercial sources and used further purification. Reactions were monitored by thin-layer chromatography carried out on silica gel plates, with detection by UV absorption (254 nm) and by heating the plates after dipping them in a solution of 12 molybdol (VI) phosphoric acid n-hydrate in 95% ethanol or ninhydrin in 97% *n*-butanol solution (2.9 % AcOH). Silica gel (particle size 40- 50 nm) was used for column chromatography. ^1H NMR spectra were collected on a 600 or 400 MHz NMR spectrometer using the deuterated solvent as an internal deuterium reference. Chemical shift data are given in δ units calibrated with residual protic solvent. The multiplicity of a signal is indicated as follows: s, singlet; d, doublet; triplet; q, quartet; quin, quintet, m, multiplet. ^{13}C NMR spectra were collected on a 150 or 100MHz spectrometer with proton decoupling using the deuterated solvent as an internal carbon reference. Chemical shift data are given in δ units calibrated with residual solvent.

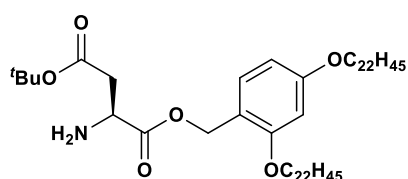
2.2 General Procedure for Synthesis of Tag-Protected Amino Acids

To a solution of tag (0.50 mmol) in DCM (10 mL), Fmoc-protected amino acid (0.75 mmol), DMAP (0.10 mmol) and DIPCI (0.75 mmol) were added. The resulting mixture was stirred for 15 min at r.t. After completion, MeCN was added to reaction solution, and concentrated under vacuum. To remaining solids, MeCN was added and filtered to give soluble tag protected amino acid as white solid quantitatively.

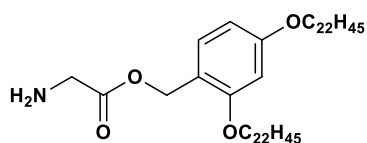
2.3 General Procedure for Deprotection of Fmoc Group

To a solution of Fmoc protected tagged amino acid (0.50 mmol) in THF (10 mL),

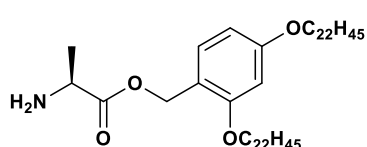
piperidine (74.2 μ L, 0.75 mmol) and DBU (1% v/v) were added. The reaction mixture was stirred for 10 min at r.t. After completion, 6 M HCl aq. was added to the solution to neutralize (pH 7.0), and then MeCN was added followed by concentration under vacuum. To remaining solid, MeCN was added and filtered to give *N*-deprotected amino acid quantitatively as white solid.



H₂N-Asp(O^tBu)-Tag (**2a**). ¹H NMR (CDCl₃, 400 MHz) δ 7.19 (1H, d, J = 7.6 Hz), 6.45-6.40 (2H, m), 5.16 (1H, d, J = 11.7 Hz), 5.12 (1H, d, J = 11.7 Hz), 3.93 (4H, t, J = 6.9 Hz), 3.76 (1H, dd, J = 7.6 Hz, 4.8 Hz), 2.72 (1H, dd, J = 16.5 Hz, 4.8 Hz), 2.60 (1H, dd, J = 16.5 Hz, 7.6 Hz), 1.81-1.68 (6H, m), 1.46-1.21 (85H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 174.5, 170.4, 160.8, 158.4, 131.2, 116.2, 104.5, 99.6, 81.1, 68.1, 62.6, 51.4, 40.1, 31.9, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.1, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₅₉H₁₀₉NO₆ 950.8147, found 950.8136.



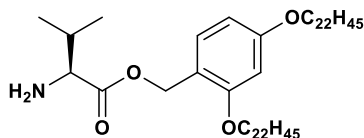
H₂N-Gly-Tag (**2b**). ¹H NMR (CDCl₃, 400 MHz) δ 7.20 (1H, d, J = 8.2 Hz), 6.46-6.40 (2H, m), 5.15 (2H, s), 3.98-3.90 (4H, m), 3.51-3.33 (2H, s), 1.81-1.71 (4H, m), 1.63-1.59 (2H, s), 1.49-1.20 (76H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ



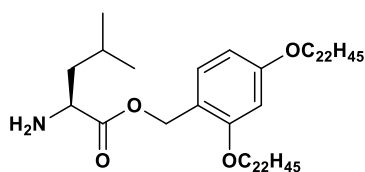
160.9, 158.5, 131.4, 116.2, 104.6, 99.8, 68.1, 62.4, 44.1, 31.9, 29.7, 29.6, 29.4, 29.3, 29.2, 26.1, 22.7, 14.1; HRMS

(ESI-MS) $[M+Na]^+$ calcd for $C_{53}H_{99}NO_4$ 836.7466, found 836.7483.

H₂N-Ala-Tag (**2c**). ¹H NMR (CDCl₃, 400 MHz) δ 7.19 (1H, d, J = 8.2 Hz), 6.46-6.40 (2H, m), 5.14 (1H, d, J = 11.9 Hz), 5.10 (1H, d, J = 11.9 Hz), 3.94 (4H, t, J = 6.4 Hz), 3.54 (1H, q, J = 6.9 Hz), 1.82-1.71 (4H, m), 1.68 (2H, s), 1.47-1.21 (79H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 176.7, 160.9, 158.5, 131.2, 116.4, 104.5, 99.7, 68.1, 62.4, 50.2, 31.9, 29.7, 29.6, 29.4, 29.3, 29.2, 26.1, 22.7, 20.6, 14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{54}H_{101}NO_4$ 850.7617, found 850.7603.

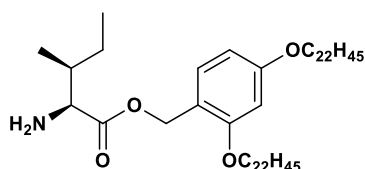


H₂N-Val-Tag (**2d**). ¹H NMR (CDCl₃, 400 MHz) δ 7.20 (1H, d, J = 8.7 Hz), 6.46-6.40 (2H, m), 5.14 (1H, d, J = 11.9 Hz), 5.10 (1H, d, J = 11.9 Hz), 3.94 (4H, t, J = 6.4 Hz), 3.29 (1H, d, J = 4.6 Hz), 2.08-1.98 (1H, m), 1.84-1.70 (4H, m), 1.65-1.58 (2H, m), 1.51-1.18 (76H, m), 0.95 (3H, d, J = 6.9 Hz), 0.92-0.84 (9H, m); ¹³C NMR (CDCl₃, 100 MHz) δ 175.7, 160.9, 158.6, 131.4, 116.4, 104.5, 99.7, 68.1, 62.2, 60.0, 32.1, 31.9, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 19.3, 17.2, 14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{56}H_{105}NO_4$ 878.7936, found 878.7946.

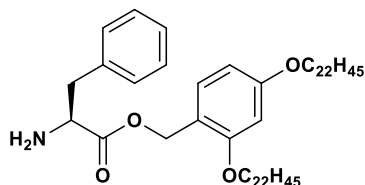


H₂N-Leu-Tag (**2e**). ¹H NMR (CDCl₃, 400 MHz) δ 7.19 (1H, d, J = 8.7 Hz), 6.46-6.40 (2H, m), 5.11 (2H, s), 3.94 (4H, t, J = 6.4 Hz), 3.46 (1H, dd, J = 8.7 Hz, 5.5 Hz), 1.81-1.71

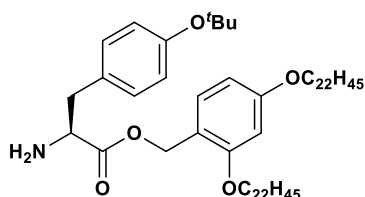
(4H, m), 1.62-1.49 (4H, m), 1.49-1.19 (77H, m), 0.94-0.84 (12H, m); ^{13}C NMR (CDCl_3 , 100 MHz) δ 176.8, 160.8, 158.5, 131.2, 116.4, 104.5, 99.7, 68.1, 62.3, 53.0, 44.0, 31.9, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 24.7, 23.0, 22.7, 21.9, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{57}\text{H}_{107}\text{NO}_4$ 892.8092, found 892.8092..



$\text{H}_2\text{N-Ile-Tag}$ (**2f**). ^1H NMR (CDCl_3 , 400 MHz) δ 7.20 (1H, d, $J = 8.7$ Hz), 6.46-6.40 (2H, m), 5.13 (1H, d, $J = 11.5$ Hz), 5.10 (1H, d, $J = 11.5$ Hz), 3.94 (4H, t, $J = 6.4$ Hz), 3.34 (1H, d, $J = 5.0$ Hz), 1.82-1.68 (5H, m), 1.61 (2H, s), 1.51-1.20 (77H, m), 1.2-1.07 (1H, m), 0.94-0.82 (12H, m); ^{13}C NMR (CDCl_3 , 100 MHz) δ 175.8, 160.8, 158.5, 131.4, 116.4, 104.5, 99.7, 68.1, 62.1, 59.2, 39.1, 31.9, 29.7, 29.6, 29.4, 29.3, 29.2, 26.1, 24.6, 22.7, 15.7, 14.1, 11.7; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{57}\text{H}_{107}\text{NO}_4$ 892.8092, found 892.8113.

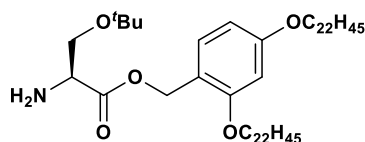


$\text{H}_2\text{N-Phe-Tag}$ (**2g**). ^1H NMR (CDCl_3 , 400 MHz) δ 7.29-7.11 (6H, m), 6.47-6.39 (2H, m), 5.14 (2H, s), 3.95 (4H, t, $J = 6.4$ Hz), 3.73 (1H, dd, $J = 7.8$ Hz, 5.0 Hz), 3.08 (1H, dd, $J = 13.7$ Hz, 5.0 Hz), 2.87 (1H, dd, $J = 13.7$ Hz, 7.8 Hz), 1.82-1.72 (4H, m), 1.55 (2H, s), 1.50-1.20 (76H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 175.2, 160.9, 158.6, 137.3, 131.5, 129.4, 128.5, 126.7, 116.2, 104.5, 99.7, 68.1, 62.4, 55.8, 40.9, 31.9, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$

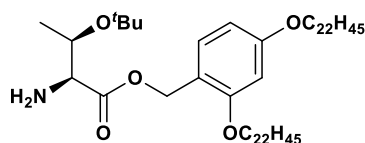


calcd for C₆₀H₁₀₅NO₄ 926.7936, found 926.7952.

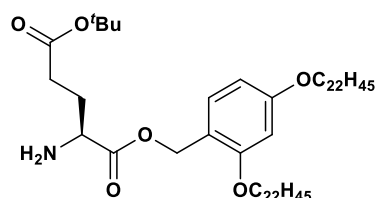
H₂N-Tyr(O^tBu)-Tag (**2h**). ¹H NMR (CDCl₃, 400 MHz) δ 7.16 (1H, d, *J* = 8.2 Hz), 7.03 (2H, d, *J* = 8.7 Hz), 6.87 (2H, d, *J* = 8.7 Hz), 6.46-6.39 (2H, m), 5.13 (2H, s), 3.99-3.90 (4H, m), 3.70 (1H, dd, *J* = 7.7 Hz, 5.0 Hz), 3.03 (1H, dd, *J* = 13.7 Hz, 5.0 Hz), 2.83 (1H, dd, *J* = 13.7 Hz, 7.3 Hz), 1.82-1.71 (4H, m), 1.58 (2H, s), 1.48-1.20 (85H, m), 0.88 (6H, t, *J* = 7.1 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 175.17, 160.9, 158.6, 154.2, 132.0, 131.4, 129.8, 124.1, 116.3, 104.5, 99.7, 78.3, 68.1, 62.4, 55.8, 40.2, 31.9, 29.7, 29.4, 29.4, 29.3, 29.2, 28.9, 26.1, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₆₄H₁₁₃NO₅ 998.8511, found 998.8529.



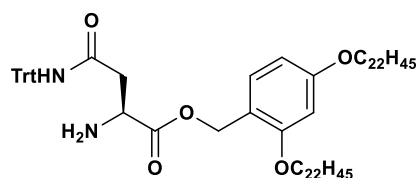
H₂N-Ser(O^tBu)-Tag (**2i**). ¹H NMR (CDCl₃, 400 MHz) δ 7.21 (1H, d, *J* = 8.3 Hz), 6.45-6.40 (2H, m), 5.18 (1H, d, *J* = 12.4 Hz), 5.13 (1H, d, *J* = 12.4 Hz), 3.94 (4H, t, *J* = 6.9 Hz), 3.64-3.54 (3H, m), 1.80-1.71 (6H, m), 1.47-1.22 (76H, m), 1.13 (9H, s), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 174.2, 160.7, 158.4, 131.0, 116.5, 104.5, 99.6, 73.0, 68.1, 63.7, 62.2, 55.3, 31.9, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 27.4, 26.1, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₆₄H₁₀₉NO₅ 922.8198, found 922.8188.



H₂N-Thr(O^tBu)-Tag (**2j**). ¹H NMR (CDCl₃, 400 MHz) δ 7.21 (1H, d, *J* = 8.3 Hz), 6.45-6.41 (2H, m), 5.20 (1H, d, *J* = 11.7 Hz), 5.01 (1H, d, *J* = 11.7 Hz), 4.01 (1H, td, *J* = 6.2 Hz, 3.4 H), 3.97-3.91 (4H, m), 3.26 (1H, d, *J* = 2.8 Hz), 1.80-1.74 (4H, m), 1.63 (2H, s), 1.47-1.20 (79H, m), 1.12 (9H, s), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 174.9, 160.9, 158.5, 131.5, 116.3, 104.5, 99.7, 73.6, 68.5, 68.1, 62.3, 60.7, 31.9, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 28.5, 26.1, 22.7, 21.0, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₅₉H₁₁₁NO₅ 936.8354, found 936.8374.

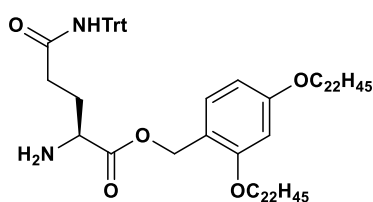


H₂N-Glu(O^tBu)-Tag (**2k**). ¹H NMR (CDCl₃, 400 MHz) δ 7.19 (1H, d, *J* = 8.7 Hz), 6.45-6.40 (2H, m), 5.13 (2H, s), 3.94 (4H, t, *J* = 6.4 Hz), 3.45 (1H, dd, *J* = 8.4 Hz, 4.8 Hz), 2.33 (2H, t, *J* = 7.3 Hz), 1.80-1.91 (1H, m), 1.87-1.71 (5H, m), 1.60 (2H, s), 1.48-1.18 (85H, m), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 175.7, 172.4, 160.9, 158.5, 131.2, 116.3, 104.5, 99.7, 80.3, 68.1, 62.4, 54.0, 31.9, 31.9, 30.0, 29.7, 29.4, 29.3, 29.2, 28.1, 26.1, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₆₀H₁₁₁NO₆ 964.8304, found 964.8309.

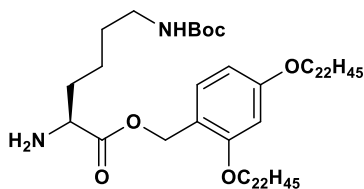


H₂N-Asn(Trt)-Tag (**2l**). ¹H NMR (CDCl₃, 400 MHz) δ 8.72 (1H, s), 7.29-7.17 (15H, m), 7.15 (1H, d, *J* = 8.2 Hz), 6.43-6.37 (2H, m), 5.16 (1H, d, *J* = 11.9 Hz), 5.11 (1H, d, *J* =

11.9 Hz), 3.92 (4H, t, $J = 6.4$ Hz), 3.83 (1H, dd, $J = 9.6$ Hz, 2.8 Hz), 2.68 (1H, dd, $J = 15.6$ Hz, 3.2 Hz), 2.51 (1H, dd, $J = 16.0$ Hz, 9.6 Hz), 1.81-1.70 (4H, m), 1.65 (2H, s), 1.48-1.21 (76H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 174.2, 169.3, 160.9, 158.4, 144.9, 131.2, 128.7, 127.9, 126.9, 115.9, 104.6, 99.7, 70.4, 68.2, 62.8, 51.7, 40.7, 31.9, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{74}\text{H}_{116}\text{N}_2\text{O}_5$ 1135.8776, found 1135.8770.

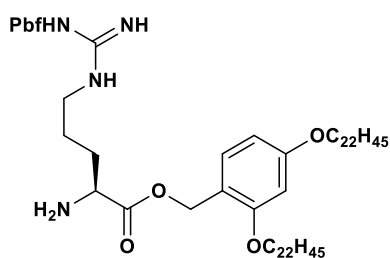


$\text{H}_2\text{N-Gln(Trt)-Tag}$ (**2m**). ^1H NMR (CDCl_3 , 400 MHz) δ 7.29-7.14 (16H, m), 7.05 (1H, s), 6.42-6.36 (2H, m), 5.14 (1H, d, $J = 11.9$ Hz), 5.09 (1H, d, $J = 11.9$ Hz), 3.94-3.84 (4H, m), 3.42 (1H, dd, $J = 8.2$ Hz, 5.0 Hz), 2.46-2.31 (2H, m), 2.11-2.01 (1H, m), 1.89-1.69 (5H, m), 1.64 (2H, s), 1.50-1.19 (76H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 175.5, 171.3, 160.9, 158.4, 144.7, 131.3, 128.7, 127.9, 126.9, 116.2, 104.6, 99.8, 70.4, 68.2, 68.1, 62.5, 53.9, 33.9, 31.9, 30.1, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{75}\text{H}_{118}\text{N}_2\text{O}_5$ 1149.8933, found 1149.8945.

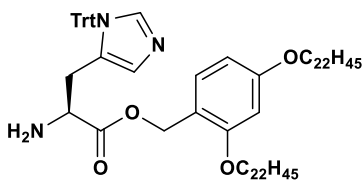


$\text{H}_2\text{N-Lys(Boc)-Tag}$ (**3n**). ^1H NMR (CDCl_3 , 400 MHz) δ 7.19 (1H, d, $J = 9.2$ Hz), 6.45-6.41 (2H, m), 5.12 (2H, s), 4.51 (1H, s), 3.94 (4H, t, $J = 6.4$ Hz), 3.42 (1H, dd, $J = 7.7$ Hz,

5.0 Hz), 3.08 (2H, m), 1.81-1.71 (5H, m), 1.58 (2H, s), 1.51-1.21 (90H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 176.1, 160.9, 158.5, 155.9, 131.2, 116.4, 104.6, 99.7, 68.1, 62.3, 54.5, 40.4, 34.4, 31.9, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 28.4, 26.1, 22.9, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{62}\text{H}_{116}\text{N}_2\text{O}_6$ 1007.8726, found 1007.8723.

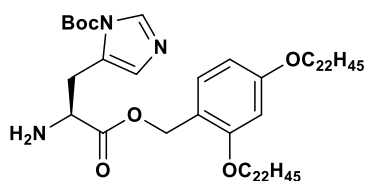


$\text{H}_2\text{N-Arg(Pbf)-Tag}$ (**30**). ^1H NMR (CDCl_3 , 600 MHz) δ 7.17 (1H, d, $J = 8.3$ Hz), 6.44-6.35 (3H, m), 6.31 (2H, s), 5.12 (1H, d, $J = 11.7$ Hz), 5.09 (1H, d, $J = 11.7$ Hz), 3.93 (4H, t, $J = 6.5$ Hz), 3.47-3.43 (1H, m), 3.20-3.06 (2H, m), 2.93 (2H, s), 2.56 (3H, s), 2.50 (3H, s), 2.08 (3H, s), 1.81-1.51 (9H, m), 1.47-1.22 (83H, s), 0.88 (6H, t, $J = 7.2$ Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 175.5, 160.9, 158.6, 158.4, 156.3, 138.3, 133.1, 132.3, 131.3, 124.5, 117.4, 116.1, 104.6, 99.7, 86.3, 68.2, 62.5, 53.9, 43.2, 40.7, 31.9, 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 28.6, 26.1, 26.0, 25.5, 22.7, 19.3, 17.9, 14.1, 12.5; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{70}\text{H}_{124}\text{N}_4\text{O}_7\text{S}$ 1187.9083, found 1187.9077.

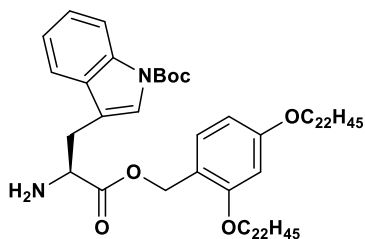


$\text{H}_2\text{N-His(Trt)-Tag}$ (**3p**). ^1H NMR (CDCl_3 , 400 MHz) δ 7.35 (1H, d, $J = 1.4$ Hz), 7.34-7.28 (9H, m), 7.14-7.09 (6H, m), 7.07 (1H, d, $J = 8.2$ Hz), 6.57 (1H, d, $J = 1.4$ Hz), 6.40 (1H, d, $J = 2.3$ Hz), 6.33 (1H, dd, $J = 8.2$ Hz, 2.3 Hz), 5.13 (1H, d, $J = 11.9$ Hz), 4.97 (1H, d, $J = 11.9$ Hz), 3.95-3.85 (4H, m), 3.77-3.71 (1H, m), 3.00 (1H, dd, $J = 14.7$ Hz, 4.2 Hz),

2.84 (1H, dd, $J = 14.7$ Hz, 7.3 Hz), 1.81-1.70 (6H, m), 1.48-1.20 (76H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 175.1, 160.6, 158.3, 142.4, 138.6, 137.4, 130.9, 129.8, 128.0, 128.0, 119.5, 116.4, 104.5, 99.7, 75.2, 68.1, 68.0, 62.2, 54.9, 33.3, 31.9, 29.7, 29.6, 29.4, 29.3, 29.2, 29.2, 26.1, 26.0, 25.6, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{76}\text{H}_{117}\text{N}_3\text{O}_4$ 1136.9117, found 1136.9132.

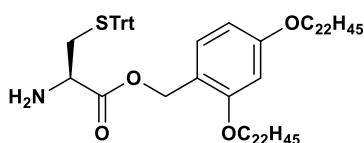


H_2N -His(Boc)-Tag (**3q**). ^1H NMR (CDCl_3 , 600 MHz) δ 8.00-7.95 (1H, s), 7.18 (1H, d, $J = 8.3$ Hz), 7.13 (1H, s), 6.44-6.40 (2H, m), 5.16 (1H, d, $J = 12.4$ Hz), 5.13 (1H, d, $J = 12.4$ Hz), 3.94 (4H, t, $J = 6.4$ Hz), 3.84 (1H, dd, $J = 8.3$ Hz, 4.8 Hz), 3.04 (1H, dd, $J = 14.4$ Hz, 4.9 Hz), 2.81 (1H, $J = 14.4$ Hz, 8.3 Hz), 1.80-1.73 (4H, m), 1.70 (2H, s), 1.60 (9H, m), 1.47-1.20 (76H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 151 MHz) δ 175.1, 160.8, 158.4, 146.9, 139.7, 136.8, 131.1, 116.3, 114.5, 104.5, 99.7, 85.4, 68.1, 68.1, 62.4, 54.2, 33.1, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 27.9, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{62}\text{H}_{111}\text{N}_3\text{O}_6$ 994.8546, found 994.8528.

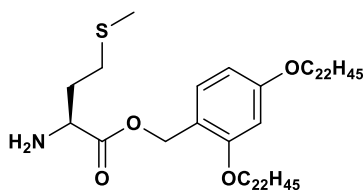


H_2N -Trp(Boc)-Tag (**3r**). ^1H NMR (CDCl_3 , 400 MHz) δ 8.12 (1H, d, $J = 6.9$ Hz), 7.54 (1H, d, $J = 7.8$ Hz), 7.46 (1H, s), 7.30 (1H, m), 7.21 (1H, m), 7.11 (1H, d, $J = 8.2$ Hz), 6.45-6.38 (2H, m), 5.16 (1H, d, $J = 11.9$ Hz), 5.11 (1H, d, $J = 11.9$ Hz), 3.94 (4H, t, $J = 6.4$ Hz), 3.83 (1H, dd, $J = 7.8$ Hz, 4.6 Hz), 3.21 (1H, dd, $J = 14.2$ Hz, 4.6 Hz), 2.95 (1H,

dd, $J = 14.6$ Hz, 8.2 Hz), 1.81-1.70 (4H, m), 1.65 (9H, s), 1.64-1.58 (2H, s), 1.51-1.20 (76H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 175.1, 160.9, 158.5, 149.6, 135.5, 131.2, 130.5, 127.1, 124.4, 124.1, 122.5, 119.0, 116.2, 115.3, 104.5, 99.7, 83.5, 68.1, 68.1, 62.6, 54.5, 31.9, 30.5, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.2, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{67}\text{H}_{114}\text{N}_2\text{O}_6$ 1065.8569, found 1065.8563.

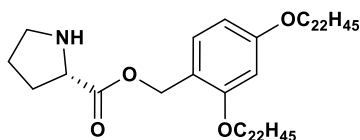


$\text{H}_2\text{N-Cys(Trt)-Tag}$ (**3s**). ^1H NMR (CDCl_3 , 400 MHz) δ 7.42-7.36 (6H, m), 7.27-7.09 (10H, m), 6.43-6.38 (2H, m), 5.07 (2H, m), 3.94 (2H, t, $J = 6.4$ Hz), 3.87 (2H, t, $J = 6.4$ Hz), 3.20 (1H, dd, $J = 8.2$ Hz, 4.6 Hz), 2.56 (1H, dd, $J = 12.4$ Hz, 4.6 Hz), 2.46 (1H, dd, $J = 12.4$ Hz, 7.8 Hz), 1.82-1.66 (4H, m), 1.60-1.18 (78 H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 173.8, 160.8, 158.3, 144.6, 131.0, 129.6, 129.6, 127.9, 127.8, 126.7, 126.6, 116.3, 104.5, 99.6, 68.1, 66.8, 62.4, 54.0, 37.0, 31.9, 29.7, 29.4, 29.4, 29.3, 29.2, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{73}\text{H}_{115}\text{NO}_4\text{S}$ 1124.8439, found 1124.8461..



$\text{H}_2\text{N-Met-Tag}$ (**3t**). ^1H NMR (CDCl_3 , 400 MHz) δ 7.20 (1H, d, $J = 8.2$ Hz), 6.45-6.39 (2H, m), 5.16 (1H, d, $J = 11.5$ Hz), 5.11 (1H, d, $J = 11.5$ Hz), 3.94 (4H, t, $J = 6.4$ Hz), 3.60 (1H, dd, $J = 8.2$ Hz, 5.0 Hz), 2.58 (2H, t, $J = 7.3$ Hz), 2.1-1.98 (4H, m), 1.94-1.70 (7H, m), 1.48-1.20 (76H, m), 0.88 (6H, t, $J = 6.6$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 175.5, 160.9, 158.6, 131.4, 116.2, 104.5, 99.7, 68.1, 62.6, 53.5, 33.8, 31.9, 30.4, 29.7, 29.6, 29.4,

29.4, 29.3, 29.2, 26.1, 22.7, 15.4, 14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{56}H_{105}NO_4S$ 910.7657, found 910.7672.



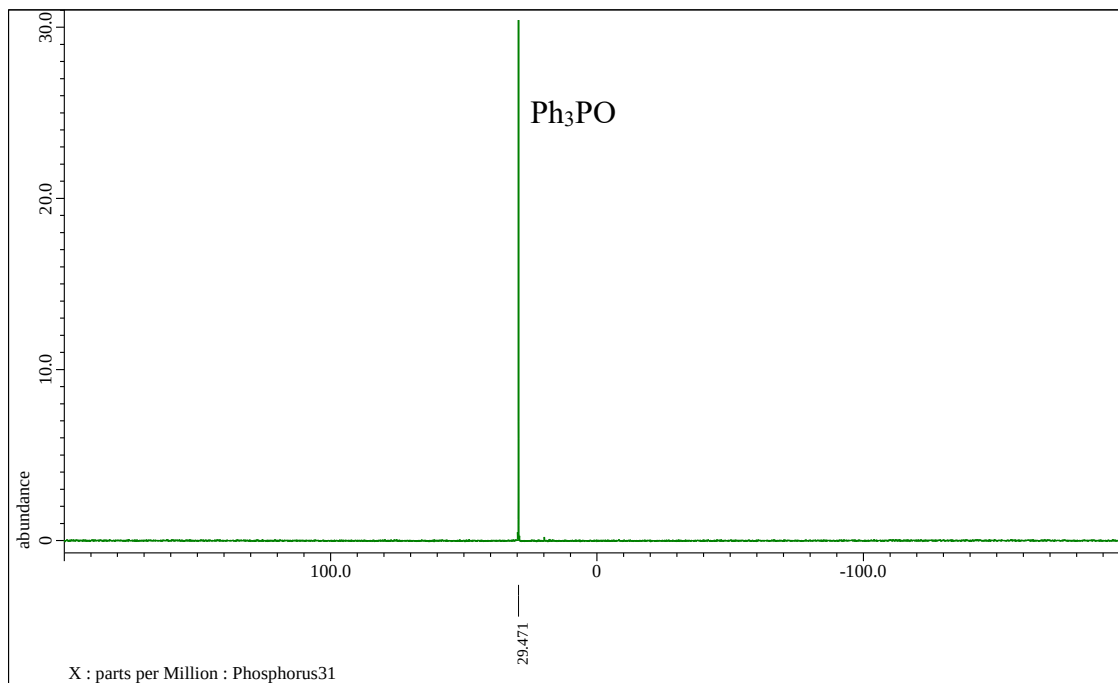
H₂N-Pro-Tag (**3u**). ¹H NMR (CDCl₃, 400 MHz) δ 7.19 (1H, d, J = 8.2 Hz), 6.45-6.41 (2H, m), 5.15 (1H, d, J = 11.9 Hz), 5.11 (1H, d, J = 11.9 Hz), 3.94 (4H, t, J = 6.4 Hz), 3.77 (1H, dd, J = 8.8 Hz, 6.0 Hz), 3.12-3.04 (1H, m), 2.93-2.85 (1H, m), 2.16-2.05 (1H, m), 1.90-1.70 (8H, m), 1.48-1.21 (76H, m), 0.88 (6H, t, J = 6.7 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 175.5, 160.9, 158.5, 131.2, 116.4, 104.5, 99.7, 68.1, 62.5, 59.8, 47.0, 31.9, 30.3, 30.0, 29.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 26.1, 25.4, 22.71, 14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{56}H_{103}NO_4$ 876.7779, found 876.7798.

2.4 General Procedure for Electrochemical Peptide Bond Formation

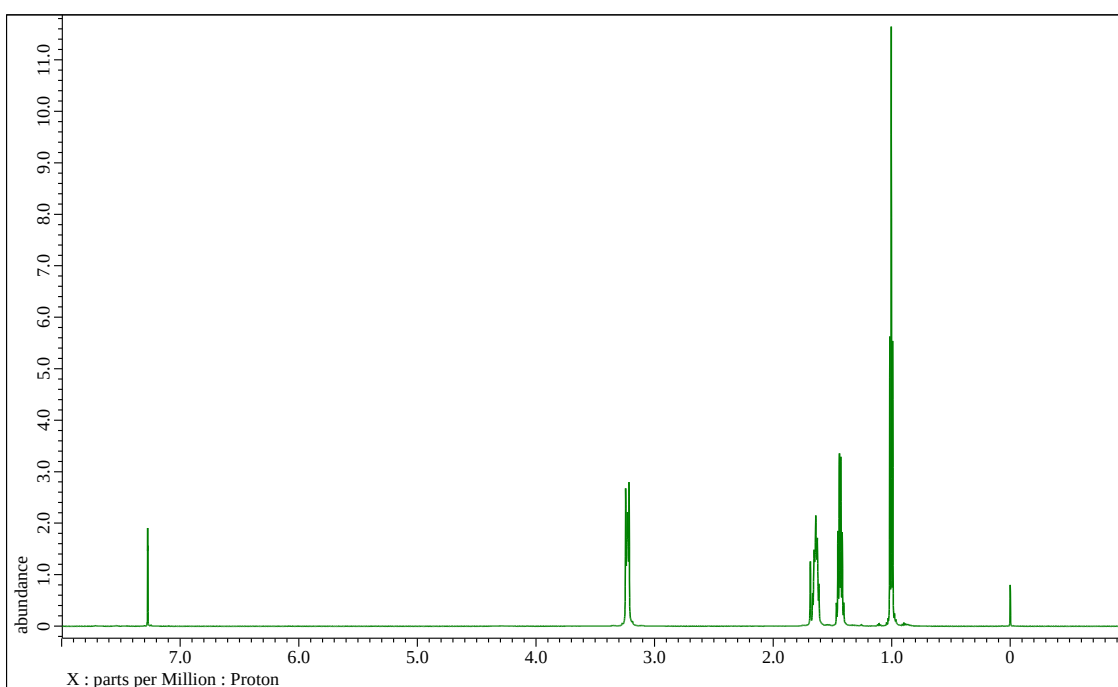
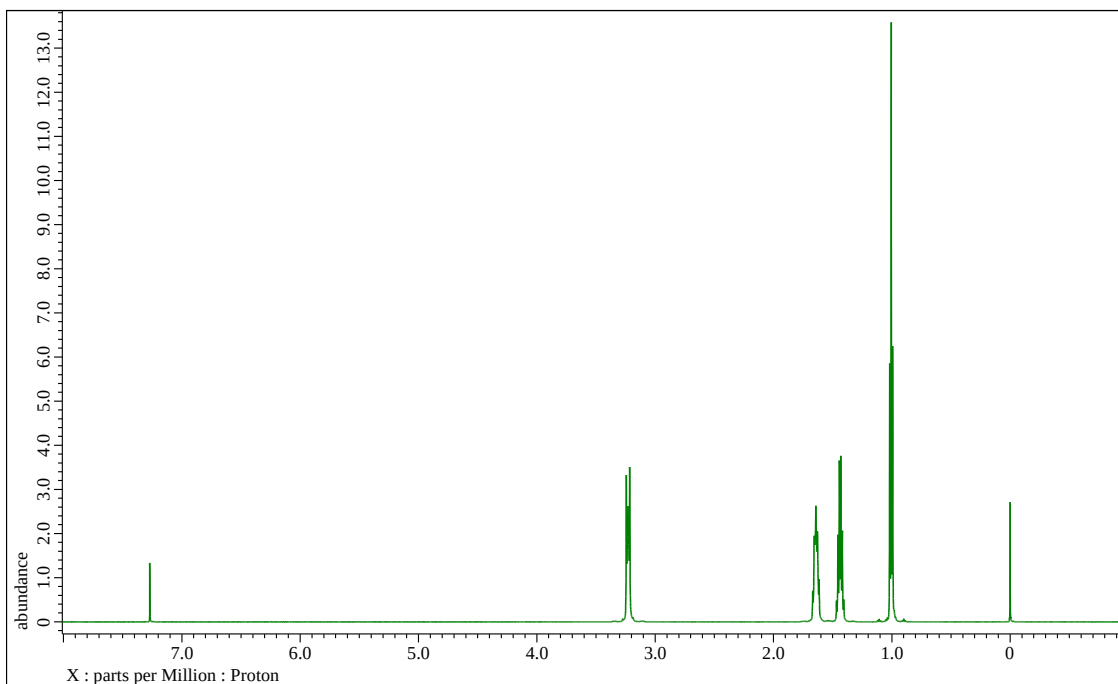
Solvent was purged with Ar gas for 2 min. To a purged solvent, 2,6-lutidine (69.9 μ L, 0.60 mmol), electrolyte (0.40 mmol), Ph₃P (0.40-0.80 mmol), Fmoc-protected amino acid (0.30-0.50 mmol), and *N*-deprotected tagged amino acid (0.20 mmol) were added. The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at rt-60 °C. After 4.8-6.0 F/mol of electricity based on *N*-deprotected tagged amino acid was passed, the reaction mixture was extracted with *c*-Hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the peptides.

2.5 Recovery of Bu₄NClO₄ and Ph₃PO

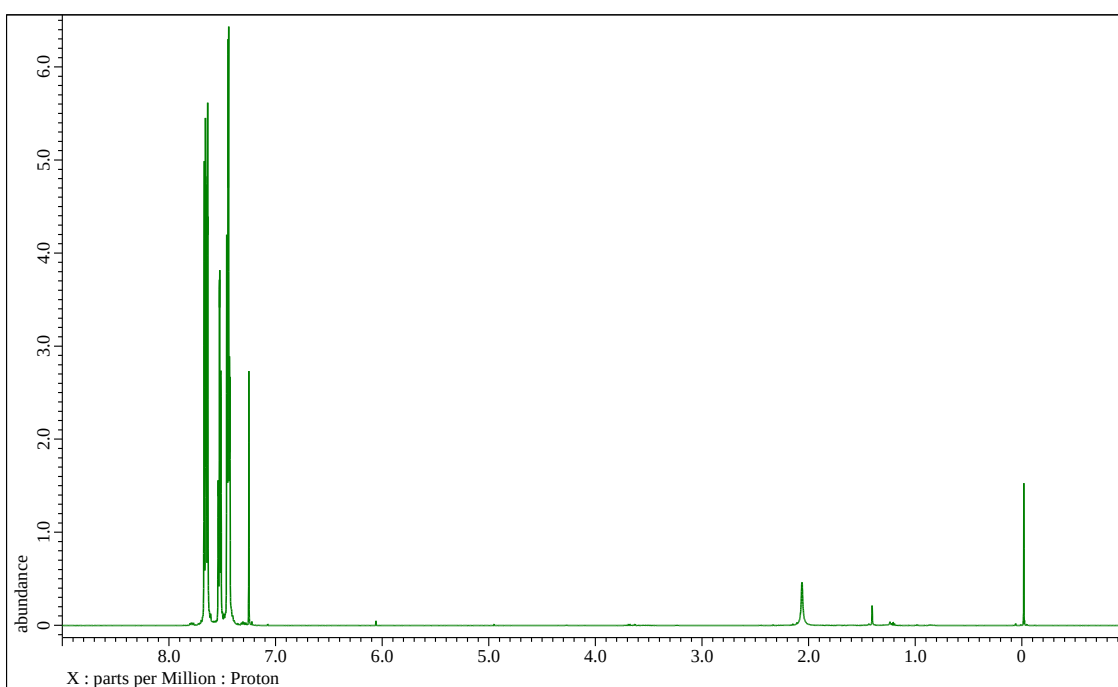
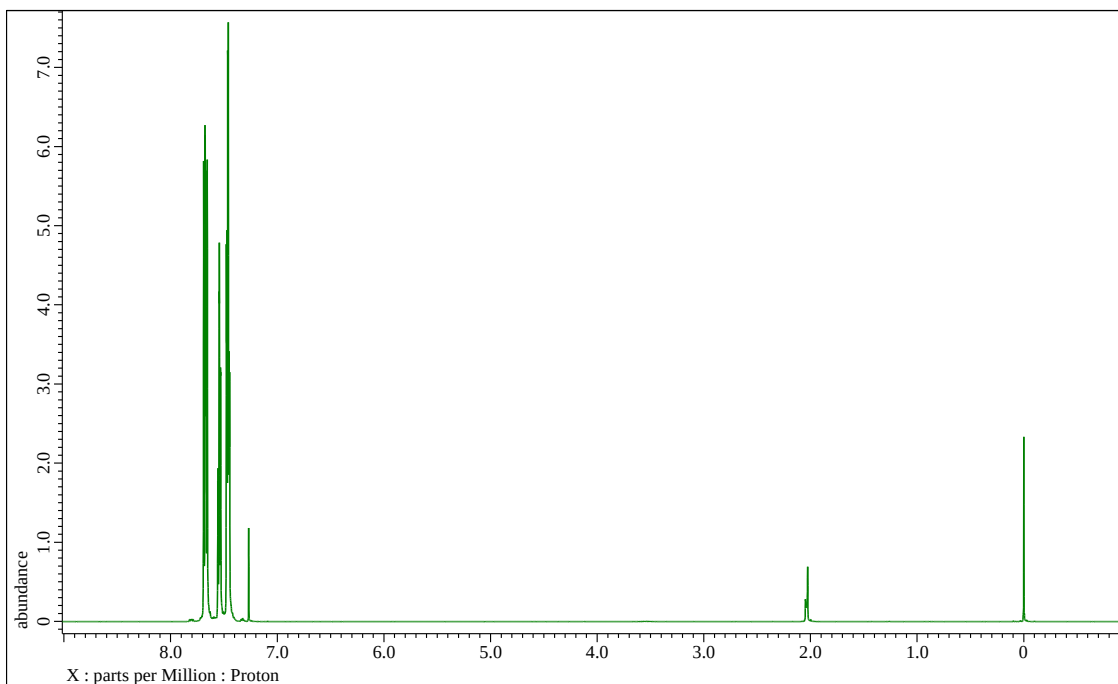
After the following the procedure **2.4**, filtrate and MeCN layer was combined followed by treatment with activated carbon. The activated carbon was removed with filtration and the resulting solution was concentrated. To the residue, toluene-*c*-Hex (30:1) 20 mL was added to afford Bu₄NClO₄ as a precipitate (quant.). After the collection of Bu₄NClO₄ by filtration, DBU (20 μ L) and piperidine (20 μ L) was added to the filtrate to deprotect Fmoc group, and stirred for 10 min at room temperature followed by addition of 1 M HCl (10 mL). Ph₃P=O was extracted with toluene (15 mL) x 2, and combined organic phase was washed with 1 M HCl (20 mL) and brine (20 mL). The organic phase was dried over anhydrous Na₂SO₄, filtered and concentrated. Crystallization with (*c*-Hex: EtOAc = 30:1) gave Ph₃P=O (101.5 mg, 91%).



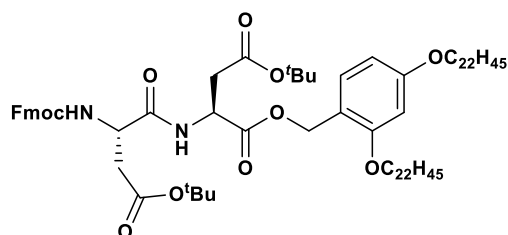
³¹P NMR analysis of reaction mixture after electrolysis under the condition of Entry 3.



Comparison between Bu_4NClO_4 from commercial source (above) and recovered (below).

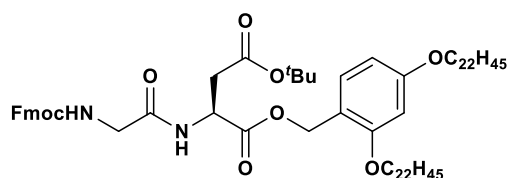


Comparison between Ph₃PO from commercial source (above) and recovered (below).



Fmoc -Asp(OtBu)-Asp(OtBu)-Tag (**3aa**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (104.9 mg, 0.40 mmol), Fmoc-Asp(OtBu)-OH (123.4 mg, 0.30 mmol), and H₂N-Asp(OtBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H₂N-Asp(OtBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 95% yield (251.1 mg) as white solid.

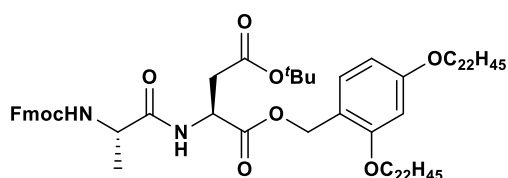
¹H NMR (CDCl₃, 600 MHz) δ 7.76 (2H, d, J = 7.6 Hz), 7.63-7.56 (2H, m), 7.45-7.35 (3H, m), 7.31 (2H, t, J = 7.6 Hz), 7.14 (1H, d, J = 8.3 Hz), 6.43-6.34 (2H, m), 5.95 (1H, d, J = 8.3 Hz), 5.19-5.11 (2H, m), 4.82-4.76 (1H, m), 4.62-4.54 (1H, m), 4.42-4.32 (2H, m), 4.22 (1H, t, J = 7.6 Hz), 3.95- 3.84 (4H, m), 2.90 (2H, m), 2.72 (1H, dd, J = 16.5, 4.1 Hz), 2.63 (1H, dd, J = 17.2, 6.2 Hz), 1.80-1.70 (4H, m), 1.48-1.20 (94H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 171.1, 170.4, 170.3, 169.6, 160.8, 158.3, 155.9, 143.9, 143.7, 141.3, 130.9, 127.7, 127.2, 127.1, 125.1, 120.0, 116.0, 104.5, 99.6, 81.8, 81.7, 68.1, 68.1, 67.3, 62.9, 51.1, 49.1, 47.1, 37.6, 37.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 28.0, 27.9, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₈₂H₁₃₂N₂O₁₁ 1343.9723, found 1392.9703.



Fmoc-Gly-Asp(OtBu)-Tag (**3ba**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Gly-OH (89.2 mg,

0.30 mmol), and H₂N-Asp(O^tBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H₂N-Asp(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 98% yield (237.0 mg) as white solid.

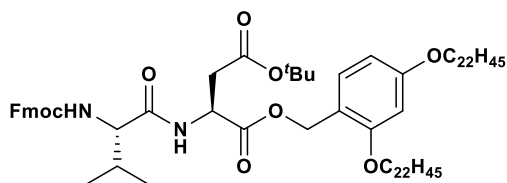
¹H NMR (CDCl₃, 600 MHz) δ 7.76 (2H, d, *J* = 7.6 Hz), 7.66-7.53 (2H, m), 7.40 (2H, t, *J* = 7.6 Hz), 7.31 (2H, t, *J* = 7.6 Hz), 7.16 (1H, d, *J* = 8.3 Hz), 6.86 (1H, d, *J* = 6.9 Hz), 6.45-6.38 (2H, m), 5.55-5.35 (1H, m), 5.21 (1H, d, *J* = 11.7 Hz), 5.14 (1H, d, *J* = 11.7 Hz), 4.86-4.79 (1H, m), 4.39 (2H, d, *J* = 6.9 Hz), 4.22 (1H, t, *J* = 7.6 Hz), 4.01-3.87 (6H, m), 2.93 (1H, dd, *J* = 17.2 Hz, 4.8 Hz), 2.75 (1H, dd, *J* = 17.2 Hz, 4.1 Hz), 1.80-1.72 (4H, m), 1.48-1.21 (85H, m), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR(CDCl₃, 150 MHz) δ 170.5, 169.9, 168.4, 160.9, 158.4, 156.4, 143.8, 143.8, 141.3, 131.1, 127.7, 127.1, 125.1, 125.1, 120.0, 115.8, 104.6, 99.7, 81.8, 68.2, 68.1, 67.3, 63.1, 48.8, 47.1, 44.3, 37.3, 31.9, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 27.9, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₇₆H₁₂₂N₂O₉ 1229.9043, found 1229.9046.



Fmoc-Ala-Asp(O^tBu)-Tag (**3ca**). Following the general procedure, 2,6-lutidine (69.9 μL, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (104.9 mg, 0.40 mmol), Fmoc-Ala-OH (93.4 mg, 0.30 mmol), and H₂N-Asp(O^tBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 50 °C. After 4.8 F/mol of electricity based on H₂N-Asp(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product

in 92% yield (225.9 mg) as white solid.

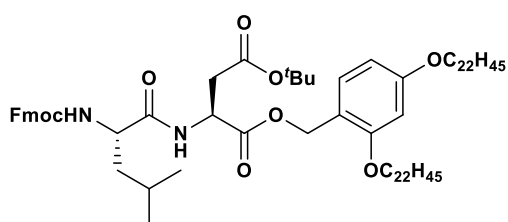
^1H NMR (CDCl_3 , 600 MHz) δ 7.76 (2H, d, J = 7.6 Hz), 7.63-7.53 (2H, m), 7.40 (2H, t, J = 7.6 Hz), 7.31 (2H, t, J = 7.6 Hz), 7.16 (1H, d, J = 8.3 Hz), 6.78 (1H, d, J = 8.3 Hz), 6.44-6.36 (2H, m), 5.44 (1H, d, J = 6.2 Hz), 5.20 (1H, d, J = 11.7 Hz), 5.14 (1H, d, J = 11.7 Hz), 4.86-4.72 (1H, m), 4.36 (2H, d, J = 6.9 Hz), 4.26 (1H, t, 7.3 Hz), 4.21 (2H, t, J = 7.2 Hz), 3.92 (4H, t, J = 4.8 Hz), 2.95 (1H, dd, J = 16.5 Hz, 4.1 Hz), 2.72 (1H, dd, J = 16.5 Hz, 4.1 Hz), 1.80-1.72 (4H, m), 1.47-1.21 (88H, m), 0.88 (6H, t, J = 7.3 Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 172.0, 170.6, 170.1, 160.9, 158.4, 155.8, 144.0, 143.9, 141.4, 131.2, 127.8, 127.2, 125.2, 120.1, 116.0, 104.6, 100.0, 81.9, 68.2, 68.2, 67.1, 63.1, 50.5, 48.9, 47.2, 37.3, 32.0, 29.8, 29.8, 29.7, 29.5, 29.5, 29.3, 29.2, 28.1, 22.8, 19.2, 14.2; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{77}\text{H}_{124}\text{N}_2\text{O}_9$ 1243.9199, found 1243.9199.



Fmoc-Val-Asp(O^tBu)-Tag (**3da**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (104.9 mg, 0.40 mmol), Fmoc-Val-OH (101.8 mg, 0.30 mmol), and $\text{H}_2\text{N-Asp}(\text{O}^t\text{Bu})\text{-Tag}$ (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/ cm^2) under Ar at 40 $^\circ\text{C}$. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Asp}(\text{O}^t\text{Bu})\text{-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 98% yield (245.7 mg) as white solid.

^1H NMR (CDCl_3 , 600 MHz) δ 7.76 (2H, d, J = 7.6 Hz), 7.64-7.56 (2H, m), 7.43-7.37 (2H, m), 7.34-7.28 (2H, m), 7.15 (1H, d, J = 8.3 Hz), 6.75 (1H, d, J = 8.9 Hz), 6.45-6.35 (2H, m), 5.45 (1H, d, 8.9 Hz), 5.18 (1H, d, 12.4 Hz), 5.14 (1H, d, 12.4 Hz), 4.89-4.80 (1H, m), 4.40 (1H, dd, J = 11.0, 7.6 Hz), 4.33 (1H, dd, J = 11.0 Hz, 7.6 Hz), 4.22 (1H, t, J = 7.6 Hz), 4.06 (1H, dd, J = 8.3, 5.5 Hz), 3.92 (4H, t, J = 6.5 Hz), 2.97 (1H, dd, J = 17.2 Hz, 4.8 Hz), 2.70 (1H, dd, J = 17.2 Hz, 4.1

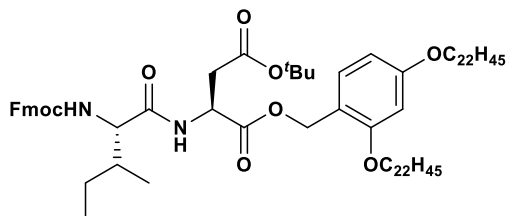
Hz), 2.15-2.05 (1H, m), 1.81-1.70 (4H, m), 1.45-1.21 (85H, m), 1.01-0.85 (12H, m); ^{13}C NMR(CDCl_3 , 150 MHz) δ 170.7, 170.5, 170.2, 160.9, 158.4, 156.2, 143.9, 143.8, 141.3, 131.2, 127.7, 127.1, 125.2, 125.1, 120.0, 115.8, 104.5, 99.6, 81.9, 68.1, 68.1, 67.1, 63.1, 60.0, 48.6, 47.2, 37.2, 31.9, 31.7, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 28.0, 26.1, 22.7, 19.0, 17.6, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{79}\text{H}_{128}\text{N}_2\text{O}_9$ 1271.9512, found 1271.9531.



Fmoc-Leu-Asp(O t Bu)-Tag (**3ea**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Val-OH (106.0 mg, 0.30 mmol), and $\text{H}_2\text{N-Asp(O}t\text{Bu)-Tag}$ (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)- c -hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/ cm^2) under Ar at 50 $^\circ\text{C}$. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Asp(O}t\text{Bu)-Tag}$ was passed, the reaction mixture was extracted with c -hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 96% yield (242.7 mg) as white solid.

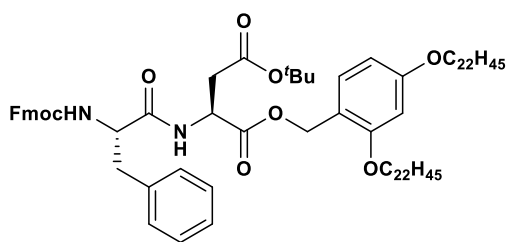
^1H NMR (CDCl_3 , 600 MHz) δ 7.76 (2H, d, $J = 7.6$ Hz), 7.59 (2H, t, $J = 6.9$ Hz), 7.40 (2H, td, $J = 7.6$ Hz, 2.8 Hz), 7.31 (2H, t, $J = 7.6$ Hz), 7.15 (1H, d, $J = 8.3$ Hz), 6.77 (1H, d, $J = 8.3$ Hz), 6.44-6.33 (2H, m), 5.24 (1H, d, $J = 8.3$ Hz), 5.18 (1H, d, $J = 11.7$ Hz), 5.15 (1H, d, $J = 11.7$ Hz), 4.86-4.75 (1H, m), 4.44-4.30 (2H, m), 4.25-4.17 (2H, t, $J = 6.9$ Hz), 3.91 (4H, m), 2.96 (1H, dd, $J = 16.5$ Hz, 4.1 Hz), 2.71 (1H, dd, $J = 16.8$, 4.1 Hz), 1.80-1.71 (4H, m), 1.71-1.58 (2H, m), 1.54-1.47 (1H, m), 1.45-1.19 (85H, m), 0.91 (6H, t, $J = 6.2$ Hz), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR(CDCl_3 , 150 MHz) δ 171.8, 170.5, 170.0, 160.8, 158.3, 156.0, 143.9, 143.8, 141.3, 131.1, 127.7, 127.1, 125.1, 120.0, 119.9, 115.9, 104.5, 99.6, 81.8, 68.1, 68.1, 67.0, 63.0, 53.4, 48.7, 47.2, 42.1, 37.3, 31.9, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 28.0, 26.1, 26.0, 24.6, 22.9, 22.7, 22.0,

14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{80}H_{130}N_2O_9$ 1285.9669, found 1285.9691.



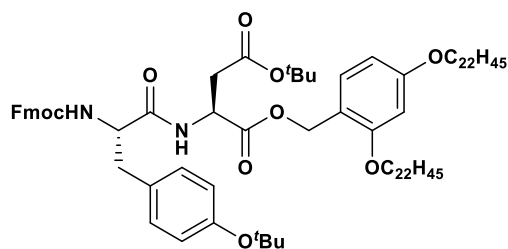
Fmoc-Ile-Asp(O^tBu)-Tag (**3fa**). Following the general procedure, 2,6-lutidine (69.9 μ l, 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Ile-OH (106.0 mg, 0.30 mmol), and H_2N -Asp(O^tBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 50 °C. After 4.8 F/mol of electricity based on H_2N -Asp(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 92% yield (233.6 mg) as white solid.

¹H NMR ($CDCl_3$, 600 MHz) δ 7.76 (2H, d, J = 7.6 Hz), 7.60 (2H, d, J = 7.6 Hz), 7.40 (2H, m), 7.31 (2H, t, J = 7.6 Hz), 7.15 (1H, d, J = 8.3 Hz), 6.73 (1H, d, J = 8.3 Hz), 6.45-6.33 (2H, m), 5.50 (1H, d, J = 8.9 Hz), 5.18 (1H, d, J = 11.7 Hz), 5.14 (1H, d, J = 11.7 Hz), 4.86-4.75 (1H, m), 4.39 (1H, dd, J = 10.7 Hz, 7.6 Hz), 4.35 (1H, dd, J = 10.7 Hz, 7.6 Hz), 4.21 (2H, t, 7.6 Hz), 4.14-4.03 (1H, m), 3.91 (4H, t, J = 6.9 Hz), 2.95 (2H, dd, J = 16.5 Hz, 4.1 Hz), 2.71 (1H, dd, J = 17.1 Hz, 4.1 Hz), 1.89-1.81 (1H, m), 1.81-1.70 (4H, m), 1.71-1.58 (2H, m), 1.51-1.22 (85H, m), 1.22 (2H, m), 0.97-0.83 (12H, m); ¹³C NMR($CDCl_3$, 150 MHz) δ 170.7, 170.6, 170.2, 160.9, 158.5, 156.1, 144.0, 143.9, 141.4, 131.2, 127.8, 127.2, 125.2, 120.0, 115.9, 104.6, 99.7, 81.9, 68.2, 68.2, 63.1, 59.5, 48.7, 47.3, 38.2, 37.3, 32.0, 29.8, 29.8, 29.7, 29.5, 29.5, 29.3, 29.2, 28.1, 26.1, 25.0, 22.8, 15.2, 14.2, 11.6; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{80}H_{130}N_2O_9$ 1285.9669, found 1285.9680.



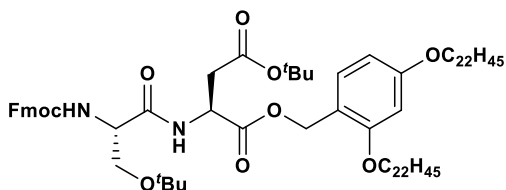
Fmoc-Phe-Asp(OtBu)-Tag (**3ga**). Following the general procedure, 2,6-lutidine (69.9 μ l, 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (104.9 mg, 0.40 mmol), Fmoc-Phe-OH (116.2 mg, 0.30 mmol), and $\text{H}_2\text{N-Asp(OtBu)-Tag}$ (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 40 °C. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Asp(OtBu)-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 97% yield (251.0 mg) as white solid.

¹H NMR (CDCl_3 , 600 MHz) δ 7.76 (2H, d, J = 7.6 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.51 (1H, d, J = 7.6 Hz), 7.39 (2H, t, J = 7.6 Hz), 7.30 (2H, t, J = 7.6 Hz), 7.26-7.19 (4H, m), 7.16 (2H, d, J = 6.9 Hz), 6.84 (1H, d, J = 6.9 Hz), 6.42-6.35 (2H, m), 5.33 (1H, d, J = 7.6 Hz), 5.19 (1H, d, J = 11.7 Hz), 5.15 (1H, d, J = 11.7 Hz), 4.82-4.72 (1H, m), 4.52-4.43 (1H, m), 4.38 (1H, dd, J = 10.9, 7.6 Hz), 4.30-4.22 (1H, m), 4.17 (1H, t, J = 6.9 Hz), 3.96-3.81 (4H, m), 3.24-2.98 (2H, m), 2.90 (1H, dd, J = 16.5 Hz, 3.4 Hz), 2.70 (1H, dd, J = 16.5 Hz, 4.1 Hz), 1.80-1.68 (4H, m), 1.45-1.20 (85H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl_3 , 150 MHz) δ 170.4, 170.4, 169.9, 160.9, 158.3, 155.7, 143.8, 143.8, 141.3, 131.1, 129.4, 128.6, 127.7, 127.1, 125.2, 125.1, 120.0, 115.9, 104.6, 99.6, 81.7, 68.2, 68.1, 67.1, 63.0, 55.7, 48.9, 47.1, 38.5, 37.3, 31.9, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{83}\text{H}_{128}\text{N}_2\text{O}_9$ 1319.9512, found 1319.9533.



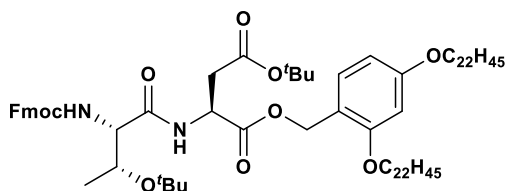
Fmoc-Tyr(O^tBu)-Asp(O^tBu)-Tag (**3ha**). Following the general procedure, 2,6-lutidine (69.9 μ l, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (104.9 mg, 0.40 mmol), Fmoc-Tyr(O^tBu)-OH (137.9 mg, 0.30 mmol), and H₂N-Asp(O^tBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H₂N-Asp(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 95% yield (261.0 mg) as white solid.

¹H NMR (CDCl₃, 600 MHz) δ 7.75 (2H, d, J = 7.6 Hz), 7.58-7.49 (2H, m), 7.39 (2H, t, J = 7.6 Hz), 7.33-7.27 (2H, m), 7.16 (1H, d, J = 7.6 Hz), 7.06 (2H, d, J = 7.6 Hz), 6.87 (2H, d, J = 7.6 Hz), 6.80 (1H, d, J = 7.6 Hz), 6.44-6.34 (2H, m), 5.33 (1H, d, J = 7.6 Hz), 5.18 (1H, d, J = 11.7 Hz), 5.15 (1H, d, J = 11.7 Hz), 4.82-4.71 (1H, m), 4.48-4.40 (1H, m), 4.39-4.32 (1H, m), 4.31-4.24 (1H, m), 4.17 (1H, t, J = 6.9 Hz), 3.94-3.83 (4H, m), 3.12-3.02 (1H, m), 3.02-2.94 (1H, m), 2.90 (1H, dd, J = 16.5, 4.1 Hz), 2.70 (1H, dd, J = 16.5, 4.1 Hz), 1.80-1.68 (4H, m), 1.45-1.21 (94H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 170.5, 170.4, 169.8, 160.8, 158.3, 155.7, 154.4, 143.8, 143.8, 141.3, 131.1, 129.8, 127.7, 127.1, 125.1, 125.1, 124.3, 120.0, 115.9, 104.6, 99.6, 81.7, 78.3, 68.2, 68.1, 67.1, 63.0, 55.9, 48.9, 47.1, 38.0, 37.3, 31.9, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.8, 27.9, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₈₇H₁₃₆N₂O₁₀ 1392.0087, found 1392.0077.



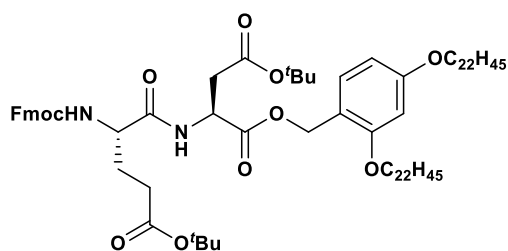
Fmoc-Ser(OtBu)-Asp(OtBu)-Tag (**3ia**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Ser(OtBu)-OH (153.4 mg, 0.40 mmol), and $\text{H}_2\text{N-Asp(OtBu)-Tag}$ (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 40 °C. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Asp(OtBu)-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 98% yield (253.1 mg) as white solid.

¹H NMR (CDCl_3 , 600 MHz) δ 7.81 (1H, d, J = 6.2 Hz), 7.76 (2H, d, J = 7.6 Hz), 7.64-7.53 (2H, m), 7.40 (2H, t, J = 7.6 Hz), 7.31 (2H, t, J = 7.6 Hz), 7.16 (1H, d, J = 7.6 Hz), 6.44-6.35 (2H, m), 5.79 (1H, d, J = 5.5 Hz), 5.20 (1H, d, J = 11.7 Hz), 5.14 (1H, d, J = 11.7 Hz), 4.85-4.79 (1H, m), 4.41-4.33 (2H, m), 4.29-4.18 (2H, m), 3.95-3.86 (4H, m), 3.84-3.76 (1H, m), 3.41 (1H, t, J = 8.6 Hz), 2.91 (1H, dd, J = 16.5 Hz, 4.8 Hz), 2.74 (1H, dd, J = 17.2 Hz, 4.8 Hz), 1.80-1.71 (4H, m), 1.46-1.18 (94H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl_3 , 150 MHz) δ 170.4, 170.2, 169.6, 160.8, 158.3, 156.0, 144.0, 143.8, 141.3, 130.9, 127.7, 127.1, 125.2, 125.2, 120.0, 116.0, 104.6, 99.6, 81.5, 74.4, 68.1, 68.1, 67.2, 62.8, 61.7, 54.2, 49.1, 47.1, 37.5, 31.9, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 27.3, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{81}\text{H}_{132}\text{N}_2\text{O}_{10}$ 1315.9774, found 1315.9796.



Fmoc-Thr(O'Bu)-Asp(O'Bu)-Tag (**3ja**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Thr(O'Bu)-OH (159.0 mg, 0.40 mmol), and H₂N-Asp(O'Bu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 40 °C. After 4.8 F/mol of electricity based on H₂N-Asp(O'Bu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 93% yield (243.3 mg) as white solid.

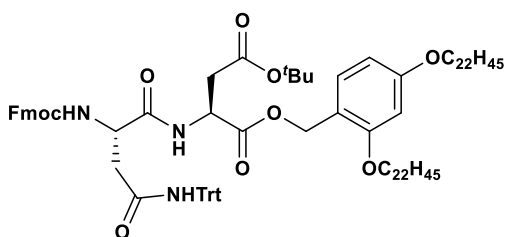
¹H NMR (CDCl₃, 600 MHz) δ 8.12 (1H, d, *J* = 7.6 Hz), 7.76 (1H, d, *J* = 7.6 Hz), 7.61 (1H, d, *J* = 7.6 Hz), 7.43-7.36 (2H, m), 7.31 (2H, t, *J* = 7.6 Hz), 7.19 (1H, d, *J* = 8.9 Hz), 6.44-6.37 (2H, m), 6.01 (1H, d, *J* = 5.5 Hz), 5.21 (1H, d, *J* = 12.4 Hz), 5.17 (1H, d, *J* = 12.4 Hz), 4.88-4.80 (1H, m), 4.42-4.32 (2H, m), 4.25-4.11 (3H, m), 3.95-3.87 (4H, m), 2.92 (1H, dd, *J* = 17.2 Hz, 4.8 Hz), 2.74 (1H, dd, *J* = 17.2 Hz, 4.1 Hz), 1.80-1.72 (4H, m), 1.47-1.20 (94H, m), 1.07 (3H, d, *J* = 6.2 Hz), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 170.5, 169.6, 169.3, 160.7, 158.3, 156.0, 144.0, 143.7, 143.7, 141.3, 141.3, 131.0, 127.7, 127.1, 125.2, 120.0, 120.0, 116.1, 104.6, 99.5, 81.4, 75.5, 68.1, 67.0, 66.6, 62.9, 58.5, 49.0, 47.2, 37.6, 31.9, 29.7, 29.6, 29.6, 29.4, 29.4, 29.4, 29.3, 29.2, 28.1, 28.0, 26.1, 22.7, 16.5, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₈₂H₁₃₄N₂O₁₀ 1329.9931, found 1329.9909.



Fmoc-Glu(O'Bu)-Asp(O'Bu)-Tag (**3ka**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (104.9 mg, 0.40 mmol), Fmoc-Glu(O'Bu)-OH (133.1 mg, 0.30 mmol), and H₂N-Asp(O'Bu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67

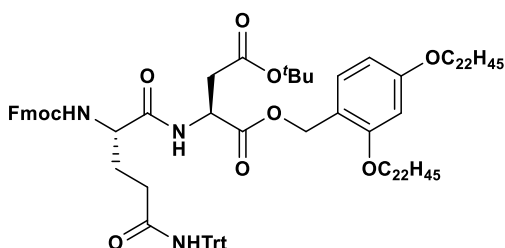
mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H₂N-Asp(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 92% yield (245.3 mg) as white solid.

¹H NMR (CDCl₃, 600 MHz) δ 7.76 (2H, d, *J* = 7.6 Hz), 7.60 (2H, m), 7.39 (2H, t, *J* = 7.6 Hz), 7.31 (2H, t, *J* = 7.6 Hz), 7.19-7.09 (2H, m), 6.44-6.35 (2H, m), 5.72 (1H, d, *J* = 7.6 Hz), 5.18 (1H, d, *J* = 12.4 Hz), 5.15 (1H, d, *J* = 12.4 Hz), 4.86-4.80 (1H, m), 4.39-4.31 (2H, m), 4.28 (1H, dd, *J* = 13.1 Hz, 7.6 Hz), 4.21 (1H, t, *J* = 7.6 Hz), 3.95-3.86 (4H, m), 2.94 (1H, dd, *J* = 17.2 Hz, 4.8 Hz), 2.72 (1H, dd, *J* = 17.2, 4.8 Hz), 2.44-2.33 (2H, m), 2.13-2.05 (1H, m), 1.96-1.86 (1H, m), 1.80-1.71 (4H, m), 1.49-1.21 (94H, m), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR(CDCl₃, 150 MHz) δ 172.7, 171.0, 170.5, 169.7, 160.8, 158.3, 156.0, 144.0, 143.8, 141.3, 131.0, 127.7, 127.1, 125.2, 125.2, 120.0, 115.9, 104.6, 99.6, 81.8, 80.9, 68.2, 68.1, 67.1, 63.0, 54.1, 48.8, 47.1, 37.3, 31.9, 31.5, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 28.6, 28.1, 28.0, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₈₃H₁₃₄N₂O₁₁ 1357.9880, found 1357.9876.



Fmoc-Asn(Trt)-Asp(O^tBu)-Tag (**31a**). Following the general procedure, 2,6-lutidine (69.9 μL, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asn(Trt)-OH (179.0 mg, 0.30 mmol), and H₂N-Asp(O^tBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H₂N-Asp(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 99% yield (300.5 mg) as white solid.

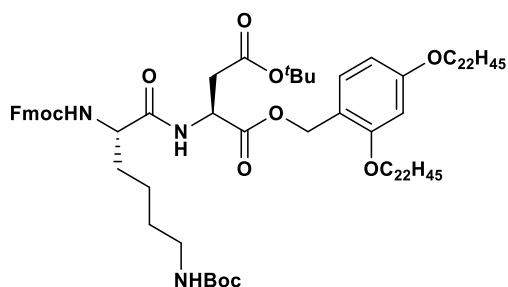
^1H NMR (CDCl_3 , 600 MHz) δ 7.75 (2H, d, J = 6.9 Hz), 7.60-7.50 (3H, m), 7.38 (2H, t, J = 7.6 Hz), 7.32-7.26 (7H, m), 7.26-7.11 (11H, m), 6.89 (1H, s), 6.43-6.34 (3H, m), 5.13 (2H, s), 4.85-4.78 (1H, m), 4.60 (1H, s), 4.38-4.27 (2H, m), 4.18 (1H, t, J = 7.2 Hz), 3.93-3.84 (4H, m), 3.09 (1H, d, J = 14.8 Hz), 2.81 (1H, dd, J = 16.5 Hz, 4.8 Hz), 2.64 (1H, dd, J = 15.8 Hz, 4.8 Hz), 2.55 (1H, dd, J = 17.2 Hz, 4.8 Hz), 1.78-1.71 (4H, m), 1.45-1.22 (85H, m), 0.88 (6H, t, J = 6.9 Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 170.7, 170.5, 170.4, 169.5, 160.7, 158.2, 156.3, 144.3, 143.9, 143.7, 141.2, 130.8, 128.7, 128.0, 127.7, 127.1, 125.3, 119.9, 116.0, 104.5, 99.6, 81.7, 70.9, 68.1, 68.1, 67.4, 62.8, 51.6, 49.0, 47.1, 38.1, 37.3, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 27.9, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{97}\text{H}_{139}\text{N}_3\text{O}_{10}$ 1529.0353, found 1529.0349.



Fmoc-Gln(Trt)-Asp(OtBu)-Tag (**3ma**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Gln(Trt)-OH (183.2 mg, 0.30 mmol), and H_2N -Asp(OtBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm 2) under Ar at room temperature. After 4.8 F/mol of electricity based on H_2N -Asp(OtBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 99% yield (301.2mg) as white solid.

^1H NMR (CDCl_3 , 600 MHz) δ 7.75 (2H, d, J = 7.6 Hz), 7.58 (2H, d, J = 6.9 Hz), 7.41-7.34 (2H, m), 7.31-7.26 (8H, m), 7.26-7.19 (9H, m), 7.17 (1H, d, J = 7.6 Hz), 7.08 (1H, d, J = 8.3 Hz), 7.02 (1H, s), 6.40 (1H, d, J = 1.4 Hz), 6.35 (1H, d, J = 8.3 Hz), 5.83 (1H, d, J = 6.9 Hz), 5.10 (1H, d, J = 11.7 Hz), 5.07 (1H, d, J = 11.7 Hz), 4.85-4.78 (1H, m), 4.38-4.28 (2H, m), 4.20 (1H, t, J = 7.2

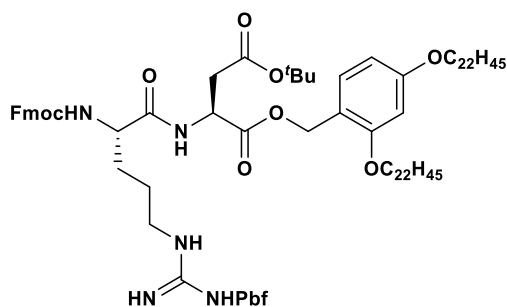
Hz), 4.18-4.111 (1H, m), 3.94-3.86 (4H, m), 2.82 (1H, dd, $J = 17.2$ Hz, 4.8 Hz), 2.68 (1H, dd, $J = 17.2$ Hz, 4.8 Hz), 2.50-2.38 (2H, m), 2.13-1.97 (2H, m), 1.80-1.69 (4H, m), 1.46-1.22 (85H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR(CDCl_3 , 150 MHz) δ 171.7, 171.1, 170.6, 169.7, 160.8, 158.3, 156.0, 144.6, 143.9, 143.8, 141.3, 141.3, 131.1, 128.8, 127.9, 127.7, 127.1, 127.0, 125.2, 119.9, 115.8, 104.5, 99.6, 81.8, 70.7, 68.2, 68.1, 67.1, 63.0, 54.0, 48.9, 47.2, 37.3, 33.0, 31.9, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 27.9, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{98}\text{H}_{141}\text{N}_3\text{O}_{10}$ 1543.0509, found 1543.0519.



Fmoc-Lys(Boc)-Asp(O t Bu)-Tag (**3na**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Lys(Boc)-OH (140.6 mg, 0.30 mmol), and H_2N -Asp(O t Bu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)- c -hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm 2) under Ar at 60 $^\circ\text{C}$. After 4.8 F/mol of electricity based on H_2N -Asp(O t Bu)-Tag was passed, the reaction mixture was extracted with c -hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 91% yield (252.0 mg) as white solid.

^1H NMR (CDCl_3 , 600 MHz) δ 7.76 (2H, d, $J = 7.6$ Hz), 7.63-7.51 (2H, m), 7.40 (2H, t, $J = 7.6$ Hz), 7.31 (2H, t, $J = 7.6$ Hz), 7.16 (1H, d, $J = 8.3$ Hz), 6.81 (1H, d, $J = 8.3$ Hz), 6.45-6.34 (2H, m), 5.51 (1H, d, $J = 6.9$ Hz), 5.16 (2H, s), 4.86-4.79 (1H, m), 4.72 (1H, s), 4.37 (2H, d, $J = 6.9$ Hz), 4.26-4.14 (2H, m), 3.97-3.85 (4H, m), 3.18-3.00 (2H, m), 2.95 (1H, dd, $J = 17.2$ Hz, 4.8 Hz), 2.70 (1H, dd, $J = 17.2$ Hz, 4.1 Hz), 1.89-1.60 (6H, m), 1.51-1.21 (98H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR(CDCl_3 , 150 MHz) δ 171.3, 171.3, 170.6, 170.0, 160.8, 158.4, 156.1, 156.0, 143.9,

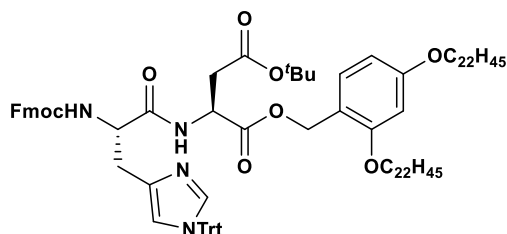
143.8, 141.3, 131.2, 127.7, 127.1, 125.2, 119.9, 115.9, 104.6, 99.6, 81.9, 79.0, 68.2, 68.1, 67.1, 63.1, 54.7, 48.7, 47.2, 39.9, 37.2, 32.6, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 29.1, 28.5, 28.0, 26.1, 26.0, 22.7, 22.2, 14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{85}H_{139}N_3O_{11}$ 1401.0302, found 1401.0320.



Fmoc-Arg(Pbf)-Asp(O'Bu)-Tag (**30a**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (157.4 mg, 0.60 mmol), Fmoc-Arg(Pbf)-OH (222.1 mg, 0.30 mmol), and H_2N -Asp(O'Bu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 50 °C. After 4.8 F/mol of electricity based on H_2N -Asp(O'Bu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 93% yield (290.1 mg) as white solid.

¹H NMR (CDCl₃, 600 MHz) δ 7.75 (2H, d, J = 7.6 Hz), 7.57 (2H, d, J = 7.6 Hz), 7.41-7.34 (2H, m), 7.32-7.26 (2H, m), 7.12 (1H, d, J = 8.3 Hz), 7.01 (1H, s), 6.42-6.34 (2H, m), 6.13-5.94 (2H, m), 5.72 (1H, s), 5.13 (2H, s), 4.91-4.84 (1H, m), 4.42-4.24 (3H, m), 4.18 (1H, t, J = 6.9 Hz), 3.91 (4H, t, J = 6.9 Hz), 3.27-3.10 (2H, m), 2.99-2.88 (3H, m), 2.69 (1H, dd, J = 17.2 Hz, 4.1 Hz), 2.60 (2.5H, s, major rotamer), 2.59 (0.5H, s, minor rotamer), 2.53 (2.5H, s, minor rotamer), 2.52 (0.5H, minor rotamer), 2.09 (2.5H, s, major rotamer), 2.08 (0.5H, s, minor rotamer), 1.78-1.71 (4H, m), 1.70-1.53 (3H, m), 1.46-1.19 (93H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 171.4, 171.3, 170.1, 160.9, 158.7, 158.3, 156.2, 143.8, 143.7, 141.3, 141.3, 138.4, 133.1, 132.3, 131.1, 127.7, 127.1, 125.1, 124.5, 120.0, 119.9, 117.4, 115.6, 104.6, 99.6, 86.3, 82.0, 68.2, 68.2,

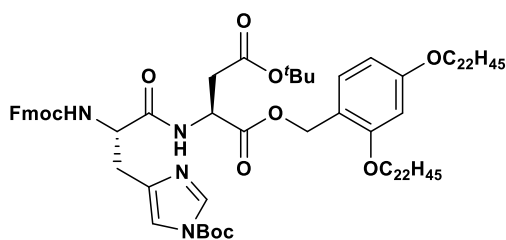
67.1, 63.3, 53.9, 48.8, 47.1, 43.2, 40.5, 40.5, 40.4, 37.1, 31.9, 30.2, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 29.1, 28.6, 27.9, 26.1, 26.0, 22.7, 19.3, 18.0, 14.1, 12.5; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{93}H_{147}N_5O_{12}S$ 1581.0659, found 1581.0668.



Fmoc-His(Trt)-Asp(O'Bu)-Tag (**3pa**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (157.4 mg, 0.60 mmol), Fmoc-His(Trt)-OH (185.9 mg, 0.30 mmol), and H_2N -Asp(O'Bu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H_2N -Asp(O'Bu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 96% yield (dr = 75:25, 294.4 mg) as white solid.

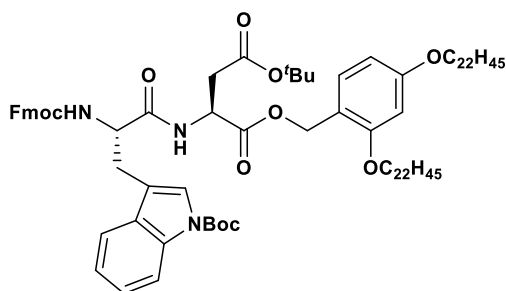
¹H NMR ($CDCl_3$, 600 MHz) δ 7.82 (1H, d, J = 7.6 Hz), 7.75 (2H, d, J = 7.6 Hz), 7.65-7.53 (2H, m), 7.41-7.34 (3H, m), 7.34-7.26 (11H, m), 7.16-7.05 (7H, m), 6.98 (0.25H, d, J = 5.5 Hz), 6.74 (0.75H, d, J = 6.2 Hz), 6.69-6.58 (1H, m), 6.45-6.27 (2H, m), 5.16-5.04 (2H, m), 4.83-4.78 (0.75H, m), 4.78-4.74 (0.25H, m), 4.54 (0.75H, dd, J = 12.7 Hz, 5.5 Hz), 4.50 (0.25H, dd, J = 11.7 Hz, 5.5 Hz), 4.35-4.27 (2H, m), 4.24-4.12 (1H, m), 3.94-3.81 (4H, m), 3.12-2.94 (2H, m), 2.92-2.81 (1H, m), 2.76-2.69 (0.25H, m), 2.64 (0.75H, dd, J = 15.8 Hz, 3.4 Hz), 1.80-1.68 (4H, m), 1.45-1.21 (85H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR ($CDCl_3$, 150 MHz) δ 171.0, 170.6, 169.5, 160.6, 158.1, 156.3, 144.0, 144.0, 144.0, 143.9, 142.4, 141.2, 138.6, 138.4, 136.9, 136.8, 132.1, 132.1, 130.7, 129.8, 128.0, 127.6, 127.1, 127.1, 125.4, 125.3, 119.9, 119.6, 119.5, 116.0, 104.5, 99.6, 99.6, 81.5, 81.4, 75.3, 68.1, 68.0, 67.2, 62.7, 55.5, 55.0, 48.9, 47.1, 37.6, 37.5, 31.9, 30.6, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 27.9, 27.9, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS)

$[M+Na]^+$ calcd for $C_{99}H_{140}N_4O_9$ 1552.0513, found 1552.0528.



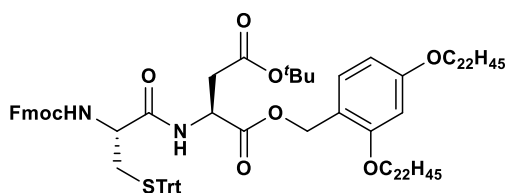
Fmoc-His(Boc)-Asp(O^tBu)-Tag (**3qa**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (157.4 mg, 0.60 mmol), Fmoc-His(Boc)-OH (143.2 mg, 0.30 mmol), and H_2N -Asp(O^tBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H_2N -Asp(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 99% yield (274.8 mg) as white solid.

1H NMR ($CDCl_3$, 600 MHz) δ 8.00 (1H, s), 7.75 (2H, d, J = 7.6 Hz), 7.64-7.50 (3H, m), 7.39 (2H, t, J = 7.2 Hz), 7.30 (2H, t, J = 6.9 Hz), 7.20 (1H, s), 7.12 (1H, d, J = 8.3 Hz), 6.47 (1H, d, J = 6.9 Hz), 6.43-6.29 (2H, m), 5.14 (1H, d, J = 11.7 Hz), 5.12 (1H, d, J = 11.7 Hz), 4.82-4.77 (1H, m), 4.63-4.48 (1H, m), 4.34 (2H, d, J = 7.6 Hz), 4.28-4.18 (1H, m), 3.94-3.82 (4H, m), 3.12 (1H, dd, J = 15.0 Hz, 4.1 Hz), 2.99 (1H, dd, J = 14.4 Hz, 5.5 Hz), 2.87 (1H, dd, J = 16.5 Hz, 4.1 Hz), 2.63 (1H, dd, J = 16.5 Hz, 3.4 Hz), 1.78-1.69 (4H, m), 1.59 (9H, s), 1.48-1.23 (85H, m), 0.88 (6H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.7, 170.4, 169.4, 160.7, 158.2, 156.1, 146.9, 144.0, 143.9, 141.3, 138.9, 136.8, 130.8, 127.6, 127.1, 127.1, 125.3, 125.3, 119.9, 116.0, 114.8, 104.5, 99.6, 85.5, 81.5, 68.1, 68.1, 67.3, 62.8, 54.6, 49.0, 47.1, 37.5, 31.9, 30.3, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 27.9, 27.9, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{85}H_{134}N_4O_{11}$ 1409.9941, found 1409.9961.



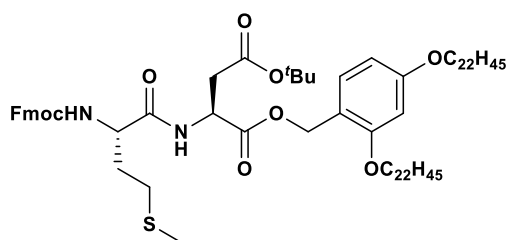
Fmoc-Trp(Boc)-Asp(O'Bu)-Tag (**3ra**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Trp(Boc)-OH (158.0 mg, 0.30 mmol), and $\text{H}_2\text{N-Asp(O'Bu)-Tag}$ (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Asp(O'Bu)-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 94% yield (271.1 mg) as white solid.

¹H NMR (CDCl_3 , 600 MHz) δ 8.13 (1H, s), 7.75 (2H, d, J = 7.6 Hz), 7.66 (1H, d, J = 7.6 Hz), 7.59-7.45 (3H, m), 7.42-7.34 (2H, m), 7.33-7.26 (3H, m), 7.22 (1H, t, J = 7.6 Hz), 7.14 (1H, d, J = 8.3 Hz), 6.74 (1H, d, J = 7.6 Hz), 6.44-6.31 (2H, m), 5.55 (1H, d, J = 6.9 Hz), 5.17 (1H, d, J = 11.7 Hz), 5.12 (1H, d, J = 11.7 Hz), 4.82-4.69 (1H, m), 4.63-4.50 (1H, m), 4.40-4.26 (2H, m), 4.25-4.13 (1H, m), 3.95-3.80 (4H, m), 3.33-3.09 (2H, m), 2.98-2.76 (1H, m), 2.71-2.54 (1H, m), 1.80-1.70 (4H, m), 1.64 (9H, s), 1.45-1.22 (85H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl_3 , 150 MHz) δ 170.5, 170.2, 169.6, 160.8, 158.3, 155.8, 149.5, 143.8, 143.8, 141.2, 135.6, 130.9, 130.2, 127.7, 127.1, 125.1, 124.9, 124.5, 122.7, 119.9, 119.0, 115.9, 115.4, 114.9, 104.5, 99.6, 83.4, 81.7, 68.1, 68.1, 67.3, 62.9, 54.7, 48.8, 47.1, 37.2, 31.9, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 28.5, 28.2, 27.8, 26.0, 26.02, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{90}\text{H}_{137}\text{N}_3\text{O}_{11}$ 1459.0145, found 1459.0140.



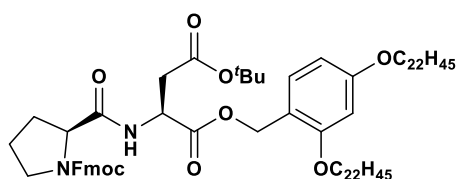
Fmoc-Cys(Trt)-Asp(OtBu)-Tag (**3sa**). Following the general procedure, 2,6-lutidine (69.9 μ l, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (157.4 mg, 0.60 mmol), Fmoc-Cys(Trt)-OH (175.7 mg, 0.30 mmol), and H₂N-Asp(OtBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 40 °C. After 4.8 F/mol of electricity based on H₂N-Asp(OtBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 95% yield (278.2 mg) as white solid.

¹H NMR (CDCl₃, 600 MHz) δ 7.78-7.71 (2H, m), 7.62-7.49 (2H, m), 7.45-7.35 (8H, m), 7.30-7.23 (8H, m), 7.22-7.17 (3H, m), 7.11 (1H, d, *J* = 8.3 Hz), 6.85 (1H, d, *J* = 6.9 Hz), 6.43-6.30 (2H, m), 5.13 (2H, s), 5.01 (1H, d, *J* = 7.6 Hz), 4.72-4.66 (1H, m), 4.40-4.26 (2H, m), 4.19 (1H, t, *J* = 6.2 Hz), 3.94-3.84 (4H, m), 3.79 (1H, dd, *J* = 13.1 Hz, 7.6 Hz), 2.85 (1H, dd, *J* = 17.1 Hz, 4.1 Hz), 2.75-2.67 (2H, m), 2.63 (1H, dd, *J* = 13.1 Hz, 4.8 Hz), 1.74 (4H, tt, *J* = 6.9 Hz), 1.45-1.21 (85H, m), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 170.3, 169.8, 169.6, 160.7, 158.2, 155.8, 144.4, 141.3, 130.8, 129.6, 128.1, 127.7, 127.1, 126.9, 125.1, 119.9, 115.9, 104.5, 99.6, 81.6, 68.1, 67.3, 62.9, 53.9, 49.0, 47.1, 37.3, 33.9, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 27.9, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₉₆H₁₃₈N₂O₉S 1518.0015, found 1518.0006.



Fmoc-Met-Asp(O^tBu)-Tag (**3ta**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (104.9 mg, 0.40 mmol), Fmoc-Met-OH (111.4 mg, 0.30 mmol), and H₂N-Asp(O^tBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 50 °C. After 4.8 F/mol of electricity based on H₂N-Asp(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 95% yield (242.7 mg) as white solid.

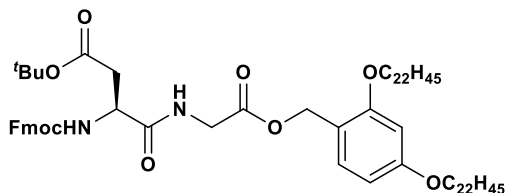
¹H NMR (CDCl₃, 600 MHz) δ 7.76 (2H, d, J = 7.6 Hz), 7.62-7.56 (2H, m), 7.40 (2H, t, J = 7.2 Hz), 7.34-7.28 (2H, m), 7.16 (1H, d, J = 7.6 Hz), 7.00 (1H, d, J = 8.9 Hz), 6.44-6.35 (2H, m), 5.59 (1H, d, J = 8.3 Hz), 5.18 (1H, d, J = 11.7 Hz), 5.14 (1H, d, J = 11.7 Hz), 4.88-4.80 (1H, m), 4.47-4.30 (3H, m), 4.21 (1H, t, J = 6.9 Hz), 3.96-3.87 (4H, m), 2.96 (1H, dd, J = 17.1 Hz, 4.8 Hz), 2.70 (1H, dd, J = 17.2 Hz, 4.8 Hz), 2.63-2.53 (2H, m), 2.09 (3H, s), 2.08-2.02 (1H, m), 2.00-1.93 (1H, m), 1.80-1.71 (4H, m), 1.46-1.20 (85H, m), 0.88 (6H, t, J = 7.2 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 170.7, 170.4, 169.9, 160.9, 158.4, 155.8, 143.9, 143.7, 141.3, 131.1, 127.7, 127.1, 125.1, 120.0, 120.0, 115.8, 104.6, 99.6, 81.9, 68.2, 68.1, 67.1, 63.1, 53.5, 48.7, 47.2, 37.3, 32.1, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.1, 26.0, 22.7, 15.0, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₇₉H₁₂₈N₂O₉S 1303.9233, found 1303.9230.



Fmoc-Pro-Asp(O^tBu)-Tag (**3ua**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), NaClO₄ (49.0 mg, 0.40 mmol), Ph₃P (209.8 mg, 0.80 mmol), Fmoc-Pro-OH (135.0 mg, 0.40 mmol), and H₂N-Asp(O^tBu)-Tag (185.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 60 °C. After 4.8 F/mol of electricity based on H₂N-Asp(O^tBu)-Tag was passed, the reaction

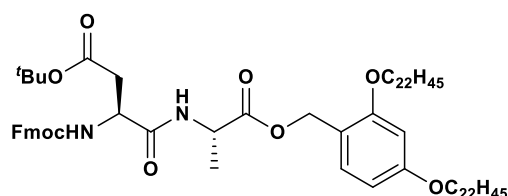
mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 98% yield (247.0 mg) as white solid.

^1H NMR (CDCl_3 , 600 MHz) δ 7.73 (2H, d, $J = 7.6$ Hz), 7.63-7.48 (2H, m), 7.42-7.33 (2H, m), 7.32-7.25 (3H, m), 7.10 (1H, brs), 6.45-6.29 (2H, m), 5.21-5.04 (2H, m), 4.82-4.70 (1H, m), 4.44-4.15 (4H, m), 3.96-3.83 (4H, m), 3.59-3.40 (2H, m), 2.85 (1H, dd, $J = 16.5$ Hz, 4.8 Hz), 2.73 (1H, dd, $J = 16.5$ Hz, 4.1 Hz), 2.22 (1H, brs), 2.12-1.99 (1H, brs), 1.96-1.81 (2H, m), 1.79-1.69 (4H, m), 1.49-1.22 (85H, m), 0.88 (6H, t, $J = 7.6$ Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 171.8, 171.5, 170.7, 170.4, 169.8, 169.8, 160.7, 158.3, 155.7, 155.1, 144.3, 144.1, 143.9, 143.8, 141.3, 131.0, 127.7, 127.0, 125.2, 119.9, 116.3, 116.1, 115.8, 104.5, 104.5, 99.6, 81.6, 81.5, 68.1, 68.1, 67.9, 67.7, 63.0, 62.9, 60.9, 60.6, 48.9, 47.5, 47.2, 47.1, 47.0, 37.5, 37.4, 31.9, 31.3, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.1, 29.0, 27.9, 26.9, 26.1, 26.0, 24.5, 23.4, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{79}\text{H}_{126}\text{N}_2\text{O}_9$ 1269.9356, found 1296.9367.



Fmoc-Asp(O^{*t*}Bu)-Gly-Tag (**3ab**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^{*t*}Bu)-OH (123.4 mg, 0.30 mmol), and H_2N -Gly-Tag (162.9 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H_2N -Gly-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 97% yield (235.4 mg) as white solid.

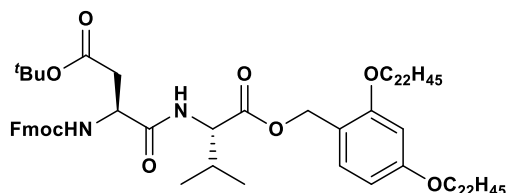
^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (2H, d, $J = 7.3$ Hz), 7.59 (2H, d, $J = 7.3$ Hz), 7.40 (2H, t, $J = 7.3$ Hz), 7.35-7.27 (2H, m), 7.18 (1H, d, $J = 8.2$ Hz), 6.99 (1H, brs), 6.44-6.37 (2H, m), 5.96 (1H, d, $J = 8.2$ Hz), 5.16 (2H, s), 4.67-4.33 (3H, m), 4.23 (1H, t, $J = 6.9$ Hz), 4.10-3.87 (6H, m), 2.91 (1H, dd, $J = 17.9$ Hz, 4.1 Hz), 2.64 (1H, dd, $J = 16.9$ Hz, 6.4 Hz), 1.80-1.70 (4H, m), 1.48-1.20 (85H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 170.5, 169.9, 168.4, 160.9, 158.4, 156.4, 143.8, 143.8, 141.3, 131.1, 127.7, 127.1, 125.1, 120.0, 115.9, 104.6, 99.6, 81.8, 68.2, 68.1, 67.3, 63.1, 48.8, 47.1, 44.3, 37.3, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 27.9, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{76}\text{H}_{122}\text{N}_2\text{O}_9$ 1229.9043, found 1229.9046.



Fmoc-Asp(OtBu)-Ala-Tag (**3ac**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Asp(OtBu)-OH (164.6 mg, 0.40 mmol), and $\text{H}_2\text{N-Ala-Tag}$ (165.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 50 $^\circ\text{C}$. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Ala-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 94% yield (230.4 mg) as white solid.

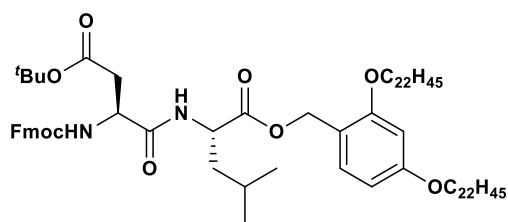
^1H NMR (CDCl_3 , 600 MHz) δ 7.76 (2H, d, $J = 7.6$ Hz), 7.59 (2H, d, $J = 6.9$ Hz), 7.40 (2H, t, $J = 7.6$ Hz), 7.31 (2H, t, $J = 7.6$ Hz), 7.16 (1H, d, $J = 8.3$ Hz), 7.12 (1H, d, $J = 6.9$ Hz), 6.45-6.37 (2H, m), 5.97 (1H, d, $J = 7.6$ Hz), 5.18 (1H, d, $J = 11.7$ Hz), 5.09 (1H, d, $J = 11.7$ Hz), 4.60-4.49 (2H, m), 4.45-4.36 (2H, m), 4.23 (1H, t, $J = 6.9$ Hz), 3.96-3.88 (4H, m), 2.92 (1H, dd, $J = 17.2$ Hz, 4.1 Hz), 2.60 (1H, dd, $J = 17.2$ Hz, 6.9 Hz), 1.79-1.71 (4H, m), 1.53-1.22 (88H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 172.5, 171.3, 170.0, 160.9, 158.4, 155.9, 143.8, 143.7,

141.3, 131.1, 127.8, 127.1, 125.1, 120.0, 115.9, 104.5, 99.7, 81.9, 68.1, 67.3, 62.9, 50.9, 48.5, 47.1, 37.7, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.0, 26.0, 22.7, 18.3, 14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{77}H_{124}N_2O_9$ 1243.9199, found 1243.9189.



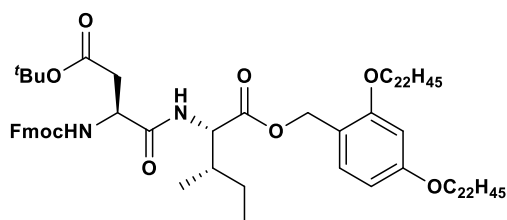
Fmoc-Asp(OtBu)-Val-Tag (**3ad**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Asp(OtBu)-OH (123.4 mg, 0.30 mmol), and H_2N -Val-Tag (171.3 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 60 °C. After 4.8 F/mol of electricity based on H_2N -Val-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 98% yield (246.9 mg) as white solid.

1H NMR ($CDCl_3$, 400 MHz) δ 7.76 (2H, d, J = 7.3 Hz), 7.59 (2H, d, J = 7.3 Hz), 7.40 (2H, t, J = 7.3 Hz), 7.31 (2H, t, J = 7.3 Hz), 7.22-7.05 (2H, m), 6.47-6.34 (2H, m), 6.05 (1H, d, J = 8.2 Hz), 5.18 (1H, d, J = 11.9 Hz), 5.06 (1H, d, J = 11.9 Hz), 4.64-4.54 (1H, m), 4.50 (1H, dd, J = 8.7 Hz, 4.6 Hz), 4.45-4.33 (2H, m), 4.23 (1H, t, J = 6.9 Hz), 3.98-3.85 (4H, m), 2.92 (1H, dd, J = 17.4 Hz, 4.1 Hz), 2.61 (1H, dd, J = 17.4 Hz, 7.3 Hz), 2.26-2.12 (1H, m), 1.81-1.68 (4H, m), 1.49-1.19 (85H, m), 0.95-0.81 (12H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.6, 171.4, 170.5, 160.9, 158.5, 155.9, 143.9, 143.7, 141.3, 131.4, 127.7, 127.1, 125.1, 120.0, 116.0, 104.5, 99.7, 81.9, 68.1, 67.3, 62.7, 57.5, 50.9, 47.1, 37.7, 31.9, 31.1, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.1, 26.0, 22.7, 19.0, 17.5, 14.1; HRMS (ESI-MS) $[M+Na]^+$ calcd for $C_{79}H_{128}N_2O_9$ 1271.9512, found 1271.9505.



Fmoc- Asp(O^tBu)-Leu-Tag (**3ae**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (123.4 mg, 0.30 mmol), and H₂N-Leu-Tag (174.1 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 50 °C. After 4.8 F/mol of electricity based on H₂N-Leu-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 96% yield (241.9 mg) as white solid.

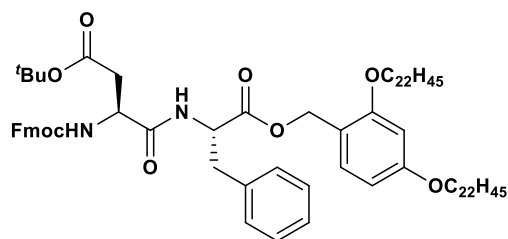
¹H NMR (CDCl₃, 400 MHz) δ 7.76 (2H, d, J = 7.3 Hz), 7.59 (2H, t, J = 7.3 Hz), 7.40 (2H, t, J = 7.3 Hz), 7.35-7.27 (2H, m), 7.16 (1H, d, J = 7.8 Hz), 6.99 (1H, d, J = 7.8 Hz), 6.46-6.35 (2H, m), 6.01 (1H, d, J = 8.2 Hz), 5.16 (1H, d, J = 11.9 Hz), 5.07 (1H, d, J = 11.9 Hz), 4.65-4.50 (2H, m), 4.40 (2H, d, J = 7.3 Hz), 4.22 (1H, t, J = 7.1 Hz), 3.92 (4H, t, J = 6.4 Hz), 2.92 (1H, dd, J = 17.4 Hz, 4.1 Hz), 2.59 (1H, dd, J = 16.9 Hz, 6.9 Hz), 1.81-1.51 (7H, m), 1.50-1.19 (85H, m), 0.92-0.82 (12H, m); ¹³C NMR(CDCl₃, 100 MHz) δ 172.5, 171.5, 170.2, 160.8, 158.4, 155.9, 143.8, 143.7, 141.3, 131.1, 127.8, 127.1, 125.1, 120.0, 116.0, 104.5, 99.6, 81.9, 68.1, 67.3, 62.7, 51.2, 50.9, 47.1, 41.5, 37.7, 31.9, 30.0, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.1, 26.0, 24.7, 22.8, 22.7, 21.9, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₈₀H₁₃₀N₂O₉ 1285.9669, found 1285.9652.



Fmoc- Asp(O^tBu)-Ile-Tag (**3fa**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60

mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (123.4 mg, 0.30 mmol), and H₂N-Ile-Tag (188.0 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 60 °C. After 4.8 F/mol of electricity based on H₂N-Ile-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 93% yield (234.4 mg) as white solid.

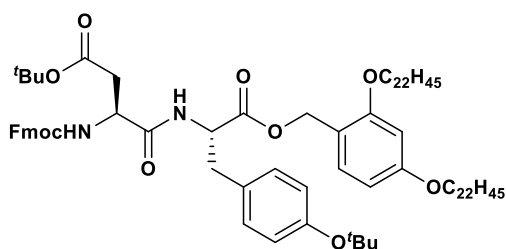
¹H NMR (CDCl₃, 400 MHz) δ 7.76 (2H, d, *J* = 7.3 Hz), 7.59 (2H, d, *J* = 7.3 Hz), 7.40 (2H, t, *J* = 7.3 Hz), 7.35-7.27 (2H, m), 7.22-7.07 (2H, m), 6.46-6.31 (2H, m), 6.05 (1H, d, *J* = 7.8 Hz), 5.17 (1H, d, *J* = 11.9 Hz), 5.06 (1H, d, *J* = 11.9 Hz), 4.63-4.48 (2H, m), 4.46-4.32 (2H, m), 4.23 (1H, t, *J* = 6.9 Hz), 3.91 (4H, t, *J* = 6.4 Hz), 2.91 (1H, dd, *J* = 17.4 Hz, 4.1 Hz), 2.61 (1H, dd, *J* = 17.4 Hz, 6.9 Hz), 1.98-1.82 (1H, m), 1.82-1.66 (4H, m), 1.49-1.20 (86H, m), 1.2-1.07 (1H, m), 0.94-0.79 (12H, m); ¹³C NMR(CDCl₃, 100 MHz) δ 171.6, 171.4, 170.3, 160.9, 158.4, 155.9, 143.9, 143.7, 141.3, 131.4, 127.7, 127.1, 125.1, 120.0, 116.0, 104.4, 99.6, 81.9, 68.1, 68.1, 67.3, 62.6, 56.9, 50.9, 47.1, 37.7, 31.9, 30.0, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.1, 24.9, 22.7, 15.5, 14.1, 11.7; HRMS (ESI-MS) [M+Na]⁺ calcd for C₈₀H₁₃₀N₂O₉ 1285.9669, found 1285.9656.



Fmoc-Asp(O^tBu)-Phe-Tag (**3ag**). Following the general procedure, 2,6-lutidine (69.9 μl, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (164.6 mg, 0.40 mmol), and H₂N-Phe-Tag (180.9 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 40 °C. After 4.8 F/mol of electricity based on H₂N-Phe-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced

with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 95% yield (245.9 mg) as white solid.

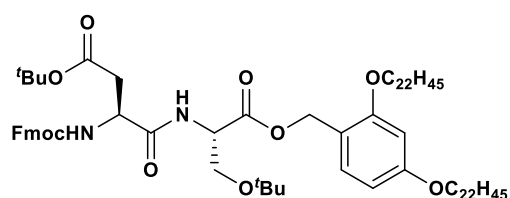
^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (2H, d, $J = 7.3$ Hz), 7.57 (2H, d, $J = 7.3$ Hz), 7.40 (2H, t, $J = 7.3$ Hz), 7.30 (2H, t, $J = 7.3$ Hz), 7.23-7.15 (3H, m), 7.12 (1H, d, $J = 8.7$ Hz), 7.09-7.03 (2H, m), 6.99 (1H, d, $J = 7.3$ Hz), 6.48-6.35 (2H, m), 5.92 (1H, d, $J = 8.2$ Hz), 5.17 (1H, d, $J = 11.9$ Hz), 5.09 (1H, d, $J = 11.9$ Hz), 4.88-4.76 (1H, m), 4.63-4.44 (1H, m), 4.43-4.28 (2H, m), 4.20 (1H, t, $J = 6.9$ Hz), 4.01-3.87 (4H, m), 3.22-3.00 (2H, m), 2.87 (1H, dd, $J = 16.9$ Hz, 4.1 Hz), 2.59 (1H, dd, $J = 16.9$ Hz, 6.4 Hz), 1.87-1.66 (4H, m), 1.50-1.20 (85H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.2, 170.9, 170.1, 161.0, 158.5, 155.9, 143.8, 143.7, 141.3, 135.7, 131.6, 129.4, 128.5, 127.7, 127.1, 127.0, 125.1, 120.0, 115.8, 104.5, 99.7, 81.8, 68.2, 68.1, 67.3, 62.9, 53.5, 50.9, 47.1, 37.6, 37.4, 31.9, 30.0, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{83}\text{H}_{128}\text{N}_2\text{O}_9$ 1319.9512, found 1319.9483.



Fmoc-Asp(OtBu)-Tyr(OtBu)-Tag (**3ah**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Asp(OtBu)-OH (164.6 mg, 0.40 mmol), and H_2N -Tyr(OtBu)-Tag (195.3 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm^2) under Ar at room temperature. After 4.8 F/mol of electricity based on H_2N -Tyr(OtBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 95% yield (261.4 mg) as white solid.

^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (2H, d, $J = 7.3$ Hz), 7.58 (2H, d, $J = 7.3$ Hz), 7.40 (2H, t, $J = 7.3$ Hz), 7.31 (2H, t, $J = 7.3$ Hz), 7.13 (1H, d, $J = 8.2$ Hz), 7.00 (1H, d, $J = 7.8$ Hz), 6.95 (2H, d,

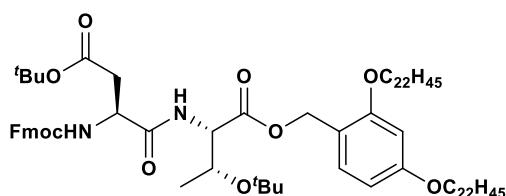
$J = 8.2$ Hz), 6.82 (2H, d, $J = 8.2$ Hz), 6.47-6.36 (2H, m), 5.92 (1H, d, $J = 7.8$ Hz), 5.16 (1H, d, $J = 11.9$ Hz), 5.09 (1H, d, $J = 11.9$ Hz), 4.85-4.75 (1H, m), 4.59-4.45 (1H, m), 4.42-4.29 (2H, m), 4.22 (1H, t, $J = 7.3$ Hz), 3.99-3.88 (4H, m), 3.13-2.97 (2H, m), 2.87 (1H, dd, $J = 17.4$ Hz, 3.7 Hz), 2.59 (1H, dd, $J = 17.4$ Hz, 6.9 Hz), 1.84-1.71 (4H, m), 1.53-1.20 (94H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR(CDCl_3 , 100 MHz) δ 171.2, 171.0, 170.0, 161.0, 158.5, 155.9, 154.4, 143.9, 143.7, 141.3, 131.6, 130.4, 129.9, 127.7, 127.1, 125.2, 124.1, 120.0, 115.9, 104.5, 99.6, 81.8, 78.2, 68.2, 68.1, 67.3, 62.8, 53.6, 50.9, 47.1, 37.5, 37.0, 31.9, 30.0, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.8, 28.0, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{87}\text{H}_{136}\text{N}_2\text{O}_{10}$ 1392.0087, found 1392.0067.



Fmoc-Asp(O'Bu)-Ser(O'Bu)-Tag (**3ai**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Asp(O'Bu)-OH (123.4 mg, 0.30 mmol), and $\text{H}_2\text{N-Ser(O'Bu)-Tag}$ (180.1 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 40 °C. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Ser(O'Bu)-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 98% yield (254.6 mg) as white solid.

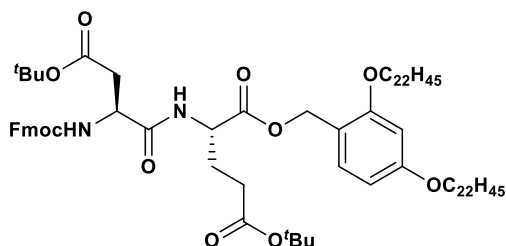
^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (2H, d, $J = 7.3$ Hz), 7.59 (2H, d, $J = 7.3$ Hz), 7.43-7.34 (3H, m), 7.31 (2H, td, $J = 7.3$ Hz, 0.9 Hz), 7.18 (1H, d, $J = 8.2$ Hz), 6.44-6.34 (2H, m), 5.99 (1H, d, $J = 7.8$ Hz), 5.16 (2H, s), 4.71-4.55 (2H, m), 4.38 (2H, d, $J = 7.3$ Hz), 4.23 (1H, t, $J = 7.3$ Hz), 3.98-3.86 (4H, m), 3.83 (1H, dd, $J = 8.7$ Hz, 2.8 Hz), 3.54 (1H, dd, $J = 8.7$ Hz, 3.2 Hz), 2.87 (1H, dd, $J = 17.4$ Hz, 4.1 Hz), 2.66 (1H, dd, $J = 16.9$ Hz, 7.3 Hz), 1.82-1.70 (4H, m), 1.48-1.20 (85H, m),

1.10 (9H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR(CDCl_3 , 100 MHz) δ 171.1, 170.5, 167.0, 160.6, 158.2, 155.8, 143.9, 143.8, 141.3, 130.8, 127.7, 127.1, 125.1, 120.0, 116.3, 104.6, 99.6, 81.8, 73.4, 68.1, 68.1, 67.3, 62.4, 61.6, 53.2, 50.7, 47.1, 38.0, 31.9, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.1, 27.2, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{81}\text{H}_{132}\text{N}_2\text{O}_{10}$ 1315.9774, found 1315.9763.



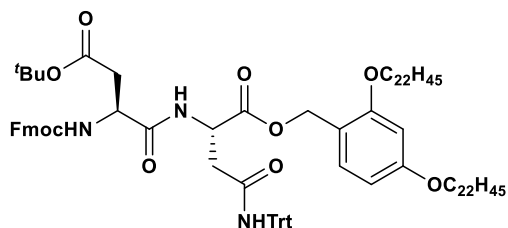
Fmoc-Asp(OtBu)-Thr(OtBu)-Tag (**3aj**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (131.1 mg, 0.50 mmol), Fmoc-Asp(OtBu)-OH (123.4 mg, 0.30 mmol), and $\text{H}_2\text{N-Thr(OtBu)-Tag}$ (182.9 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm^2) under Ar at 40 $^\circ\text{C}$. The product was obtained in 95% yield (249.5 mg) as white solid.

^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (2H, d, $J = 7.3$ Hz), 7.60 (2H, d, $J = 7.3$ Hz), 7.39 (2H, t, $J = 7.3$ Hz), 7.35-7.27 (3H, m), 7.18 (1H, d, $J = 8.7$ Hz), 4.46-6.37 (2H, m), 6.03 (1H, d, $J = 7.8$ Hz), 5.15 (1H, d, $J = 11.9$ Hz), 5.03 (1H, d, $J = 11.9$ Hz), 4.75-4.57 (1H, m), 4.47 (1H, dd, $J = 9.2$ Hz, 1.4 Hz), 4.43-4.30 (2H, m), 4.29-4.17 (2H, m), 3.99-3.85 (4H, m), 2.88 (1H, dd, $J = 17.4$ Hz, 4.1 Hz), 2.66 (1H, dd, $J = 17.4$ Hz, 6.9 Hz), 1.81-1.70 (4H, m), 1.49-1.21 (85H, m), 1.16 (3H, d, $J = 6.4$ Hz), 1.08 (9H, s), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR(CDCl_3 , 100 MHz) δ 171.2, 171.0, 170.4, 160.8, 158.4, 155.8, 143.9, 143.8, 141.3, 131.4, 127.7, 127.1, 125.2, 120.0, 115.9, 104.6, 99.6, 81.6, 73.9, 68.1, 68.1, 67.3, 67.1, 62.6, 58.2, 50.9, 47.2, 38.1, 31.9, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 28.3, 28.1, 26.1, 22.7, 21.1, 20.0, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{82}\text{H}_{134}\text{N}_2\text{O}_{10}$ 1329.9931, found 1329.9918.



Fmoc-Asp(O^tBu)-Glu(O^tBu)-Tag (**3ak**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (164.6 mg, 0.40 mmol), and H₂N-Glu(O^tBu)-Tag (188.6 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H₂N-Thr(O^tBu)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 95% yield (254.3 mg) as white solid.

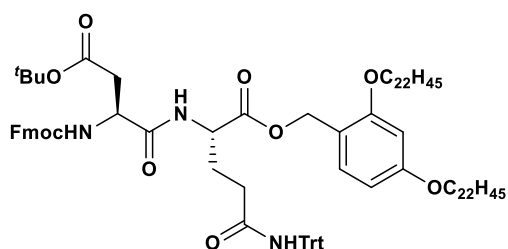
¹H NMR (CDCl₃, 600 MHz) δ 7.76 (2H, d, J = 7.6 Hz), 7.66-7.51 (2H, m), 7.40 (2H, t, J = 7.6 Hz), 7.31 (2H, t, J = 7.6 Hz), 7.25-7.11 (2H, m), 6.46-6.34 (2H, m), 5.99 (1H, d, J = 8.3 Hz), 5.19 (1H, d, J = 11.7 Hz), 5.09 (1H, d, J = 11.7 Hz), 4.65-4.52 (2H, m), 4.41 (2H, d, J = 6.9 Hz), 4.23 (1H, t, J = 6.9 Hz), 3.97-3.85 (4H, m), 2.96 (1H, dd, J = 17.3 Hz, 3.4 Hz), 2.59 (1H, dd, J = 17.3 Hz, 5.5 Hz), 2.35-2.11 (3H, m), 2.01-1.88 (1H, m), 1.80-1.71 (4H, m), 1.53-1.20 (94H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 172.0, 171.4, 170.4, 160.9, 158.4, 155.9, 143.9, 143.7, 141.3, 131.2, 127.8, 127.1, 125.1, 120.0, 115.9, 104.5, 99.7, 81.9, 80.5, 68.1, 68.1, 67.3, 63.0, 52.1, 51.0, 47.1, 37.6, 31.9, 31.2, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 28.1, 27.5, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₈₃H₁₃₄N₂O₁₁ 1357.9880, found 1357.9891.



Fmoc-Asp(O^tBu)-Asn(Trt)-Tag (**3al**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60

mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (123.4 mg, 0.30 mmol), and H₂N-Asn(Trt)-Tag (222.8 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H₂N-Asn(Trt)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 96% yield (289.9 mg) as white solid.

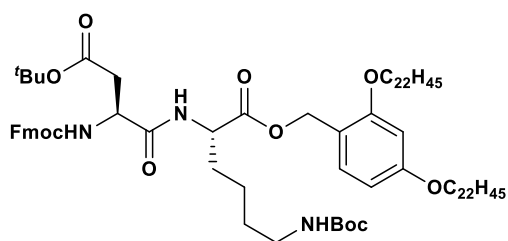
¹H NMR (CDCl₃, 400 MHz) δ 7.75 (2H, d, *J* = 7.3 Hz), 7.63-7.43 (3H, m), 7.37 (2H, d, *J* = 7.3 Hz), 7.29-7.10 (17H, m), 7.04 (1H, d, *J* = 8.2 Hz), 6.70 (1H, s), 6.39 (1H, d, *J* = 1.8 Hz), 6.31 (1H, dd, *J* = 8.2 Hz, 1.8 Hz), 5.78 (1H, d, *J* = 8.2 Hz), 5.13 (1H, d, *J* = 11.9 Hz), 5.06 (1H, d, *J* = 11.9 Hz), 4.83-4.74 (1H, m), 4.60-4.46 (1H, m), 4.32 (2H, d, *J* = 7.3 Hz), 4.18 (1H, t, *J* = 7.3 Hz), 3.95-3.79 (4H, m), 3.03 (1H, dd, *J* = 15.6 Hz, 4.6 Hz), 2.89-2.70 (2H, m), 2.60 (1H, dd, *J* = 16.5 Hz, 5.0 Hz), 1.79-1.68 (4H, m), 1.46-1.20 (85H, m), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR(CDCl₃, 100 MHz) δ 171.5, 171.4, 170.9, 170.7, 160.9, 158.4, 156.0, 144.7, 143.8, 143.6, 141.3, 131.2, 128.7, 127.8, 127.8, 127.1, 126.9, 125.1, 120.0, 115.8, 104.6, 99.7, 81.9, 70.5, 68.2, 68.1, 67.3, 63.0, 52.0, 47.1, 37.4, 33.3, 31.9, 29.7, 29.4, 29.4, 29.3, 29.1, 28.0, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₉₇H₁₃₉N₃O₁₀ 1529.0353, found 1529.0337.



Fmoc-Asp(O^tBu)-Gln(Trt)-Tag (**3am**). Following the general procedure, 2,6-lutidine (69.9 μl, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (123.4 mg, 0.30 mmol), and H₂N-Asn(Trt)-Tag (225.6 mg, 0.20 mmol) were added to Ar-

purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H₂N-Gln(Trt)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 93% yield (282.0 mg) as white solid.

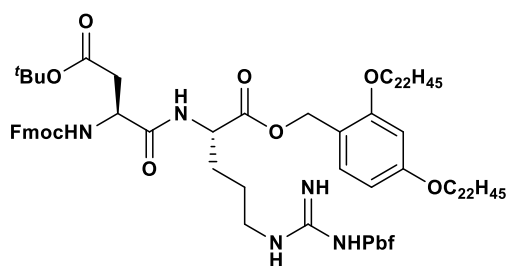
¹H NMR (CDCl₃, 400 MHz) δ 7.75 (2H, d, *J* = 7.3 Hz), 7.62-7.50 (2H, m), 7.39 (2H, t, *J* = 7.3 Hz), 7.33-7.26 (2H, m), 7.24-7.13 (18H, m), 6.43-6.33 (2H, m), 5.85 (1H, d, *J* = 8.2 Hz), 5.17 (1H, d, *J* = 11.9 Hz), 5.10 (1H, d, *J* = 11.9 Hz), 4.66-4.56 (1H, m), 4.56-4.46 (1H, m), 4.38 (2H, d, *J* = 6.0 Hz), 4.20 (1H, t, *J* = 6.9 Hz), 3.95-3.82 (4H, m), 2.94 (1H, dd, *J* = 17.5 Hz, 4.1 H), 2.59 (1H, dd, *J* = 17.5 Hz, 4.6 Hz), 2.41-2.16 (3H, m), 1.95-1.81 (1H, m), 1.80-1.67 (4H, m), 1.49-1.20 (85H, m), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR(CDCl₃, 100 MHz) δ 170.5, 170.4, 169.1, 160.6, 158.0, 155.9, 144.4, 144.0, 143.7, 141.2, 130.7, 128.7, 128.0, 127.7, 127.1, 125.2, 119.9, 116.0, 104.6, 99.6, 81.6, 70.9, 68.1, 68.1, 67.3, 62.9, 51.4, 49.5, 47.0, 38.3, 37.9, 31.9, 30.0, 29.7, 29.4, 29.3, 29.1, 28.0, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₉₈H₁₄₁N₃O₁₀ 1543.0509, found 1543.0511.



Fmoc-Asp(O^tBu)-Lys(Boc)-Tag (**3an**). Following the general procedure, 2,6-lutidine (69.9 μL, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (123.4 mg, 0.30 mmol), and H₂N-Lys(Boc)-Tag (197.1 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 50 °C. After 4.8 F/mol of electricity based on H₂N-Lys(Boc)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with

MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 98% yield (255.6 mg) as white solid.

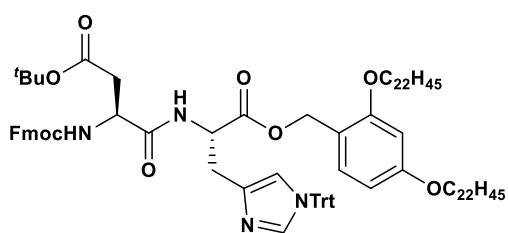
^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (2H, d, J = 7.3 Hz), 7.59 (2H, d, J = 7.3 Hz), 7.39 (2H, t, J = 7.3 Hz), 7.35-7.27 (2H, m), 7.16 (1H, d, J = 8.2 Hz), 7.08 (1H, d, J = 7.8 Hz), 6.45-6.36 (2H, m), 6.15-5.83 (1H, m), 5.17 (1H, d, J = 11.9 Hz), 5.09 (1H, d, J = 11.9 Hz), 4.68-4.49 (3H, m), 4.41 (2H, d, J = 7.3 Hz), 4.23 (1H, t, J = 6.9 Hz), 3.97-3.86 (4H, m), 3.09-2.97 (2H, m), 2.93 (1H, dd, J = 17.4 Hz, 4.6 Hz), 2.62 (1H, dd, J = 17.4 Hz), 1.91-1.62 (6H, m), 1.50-1.21 (98H, m), 0.88 (6H, t, J = 6.9 Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.8, 171.3, 170.3, 160.9, 158.4, 156.0, 155.9, 143.9, 143.7, 141.3, 131.2, 127.8, 127.1, 125.1, 120.0, 115.9, 104.6, 99.7, 81.9, 79.0, 68.2, 68.1, 67.3, 62.8, 52.3, 51.0, 47.1, 40.23, 37.6, 31.9, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.4, 28.0, 26.1, 26.0, 22.7, 22.2, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{85}\text{H}_{139}\text{N}_3\text{O}_{11}$ 1401.0302, found 1401.0276.



Fmoc-Asp(OtBu)-Arg(Pbf)-Tag (**3ao**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (157.4 mg, 0.60 mmol), Fmoc-Asp(OtBu)-OH (123.4 mg, 0.30 mmol), and $\text{H}_2\text{N-Arg(Pbf)-Tag}$ (197.1 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm 2) under Ar at 50 $^\circ\text{C}$. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Arg(Pbf)-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 95% yield (296.7 mg) as white solid.

^1H NMR (CDCl_3 , 400 MHz) δ 7.74 (2H, d, J = 7.8 Hz), 7.61-7.52 (2H, m), 7.38 (2H, t, J = 7.3

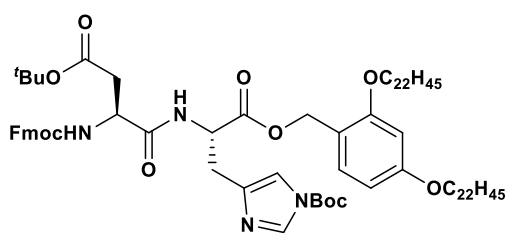
Hz), 7.32-7.26 (2H, m), 7.13 (1H, d, $J = 8.2$ Hz), 6.44-6.36 (2H, m), 6.18-5.77 (4H, m), 5.16 (1H, d, $J = 11.9$ Hz), 5.08 (1H, d, $J = 11.9$ Hz), 4.64-4.46 (2H, m), 4.38 (2H, d, $J = 6.9$ Hz), 4.18 (1H, t, $J = 6.9$ Hz), 3.94-3.85 (4H, m), 3.26-3.04 (2H, m), 2.93-2.81 (3H, m), 2.64 (1H, dd, $J = 16.9$ Hz, 4.1 Hz), 2.56 (3H, s), 2.50 (3H, s), 2.06 (3H, s), 1.92-1.63 (7H, m), 1.60-1.21 (93H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR(CDCl_3 , 100 MHz) δ 171.5, 171.0, 171.0, 161.0, 158.6, 158.4, 156.3, 156.0, 143.8, 143.5, 141.3, 138.4, 133.2, 132.3, 132.0, 131.3, 127.8, 127.1, 125.1, 124.5, 120.0, 117.4, 115.6, 104.6, 99.7, 86.2, 82.2, 68.2, 68.1, 67.4, 63.1, 51.8, 51.4, 47.0, 43.2, 40.6, 37.4, 31.9, 30.2, 29.7, 29.7, 29.5, 29.4, 29.3, 29.1, 28.6, 28.0, 26.1, 26.0, 24.6, 22.7, 19.2, 17.9, 14.1, 12.4; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{93}\text{H}_{147}\text{N}_5\text{O}_{12}\text{S}$ 1581.0659, found 1581.0657..



Fmoc-Asp(OtBu)-His(Trt)-Tag (**3ap**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (157.4 mg, 0.60 mmol), Fmoc-Asp(OtBu)-OH (123.4 mg, 0.30 mmol), and H_2N -His(Trt)-Tag (227.3 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H_2N -His(Trt)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 97% yield (297.9 mg) as white solid.

^1H NMR (CDCl_3 , 400 MHz) δ 8.12 (0.4H, d, $J = 7.3$ Hz, minor rotamer), 7.90 (0.6H, d, $J = 7.8$ Hz, major rotamer), 7.73 (2H, d, $J = 7.3$ Hz), 7.61-7.49 (2H, m), 7.36 (2H, t, $J = 7.3$ Hz), 7.31-7.25 (3H, m), 7.25-7.17 (9H, m), 7.08-6.93 (7H, m), 6.56-6.48 (1H, m), 6.48-6.41 (1H, m), 6.37

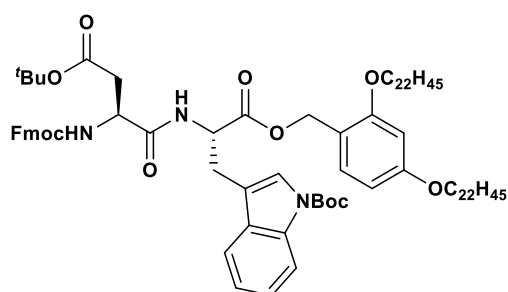
(1H, d, $J = 1.8$ Hz), 6.26 (1H, dd, $J = 8.2$ Hz, 1.8 Hz), 5.09 (1H, d, $J = 11.9$ Hz), 5.01-4.87 (1H, m), 4.86-4.75 (1H, m), 4.69-4.56 (1H, m), 4.37-4.21 (2H, m), 4.15 (0.4H, t, $J = 6.9$ Hz, minor rotamer), 4.07 (0.6H, t, $J = 6.9$ Hz, major rotamer), 3.90-3.79 (4H, m), 3.12-2.95 (2H, m), 2.94-2.58 (2H, m), 1.79-1.64 (4H, m), 1.46-1.21 (85H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.9, 170.8, 170.7, 170.5, 170.4, 170.3, 170.2, 170.2, 170.1, 160.6, 160.5, 158.1, 158.1, 155.9, 155.9, 155.8, 144.0, 144.0, 143.9, 143.9, 143.8, 143.7, 143.7, 142.3, 142.2, 141.3, 138.7, 138.6, 136.5, 136.4, 130.6, 130.6, 129.7, 128.0, 127.7, 127.1, 127.1, 125.3, 125.3, 125.2, 119.9, 119.8, 119.5, 116.3, 116.2, 104.5, 99.6, 81.5, 81.3, 75.2, 75.2, 68.1, 68.0, 67.3, 67.1, 62.4, 62.4, 53.0, 52.9, 51.6, 51.4, 47.1, 37.7, 31.9, 30.0, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 28.1, 28.0, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{99}\text{H}_{140}\text{N}_4\text{O}_9$ 1552.0513, found 1552.0502.



Fmoc-Asp(OtBu)-His(Boc)-Tag (**3aq**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (157.4 mg, 0.60 mmol), Fmoc-Asp(OtBu)-OH (123.4 mg, 0.30 mmol), and H_2N -His(Boc)-Tag (198.9 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 4.8 F/mol of electricity based on H_2N -His(Boc)-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 99% yield (274.8 mg) as white solid.

^1H NMR (CDCl_3 , 600 MHz) δ 7.88 (1H, s), 7.76 (2H, d, $J = 7.6$ Hz), 7.67 (1H, d, $J = 7.6$ Hz), 7.61 (2H, t, $J = 6.9$ Hz), 7.39 (2H, t, $J = 7.6$ Hz), 7.30 (2H, t, $J = 7.6$ Hz), 7.13 (1H, d, $J = 8.3$ Hz), 7.06 (1H, s), 6.44-6.36 (2H, m), 6.13 (1H, d, $J = 8.3$ Hz), 5.14 (1H, d, $J = 12.4$ Hz), 5.11 (1H, d,

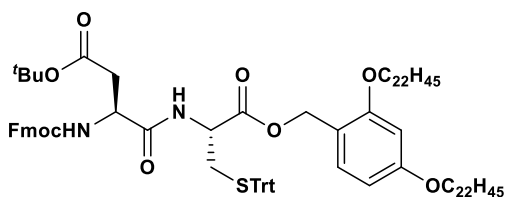
$J = 12.4$ Hz), 4.86-4.81 (1H, m), 4.66-4.58 (1H, m), 4.38 (2H, d, $J = 6.9$ Hz), 4.24 (1H, t, $J = 6.9$ Hz), 3.96-3.88 (4H, m), 3.06 (2H, d, $J = 5.5$ Hz), 2.89 (1H, dd, $J = 17.2$ Hz, 4.8 Hz), 2.66 (1H, dd, $J = 17.2$ Hz, 6.2 Hz), 1.80-1.73 (4H, m), 1.55 (9H, s), 1.48-1.21 (85H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 171.0, 170.7, 170.3, 160.7, 158.3, 155.9, 146.7, 143.9, 143.8, 141.3, 138.4, 136.8, 131.0, 127.7, 127.1, 125.2, 120.0, 116.1, 114.7, 104.5, 99.6, 85.4, 81.5, 68.2, 68.1, 67.3, 62.7, 52.4, 51.2, 47.2, 37.7, 31.9, 29.7, 29.7, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 27.8, 26.1, 26.1, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{85}\text{H}_{134}\text{N}_4\text{O}_{11}$ 1409.9941, found 1409.9939.



Fmoc-Asp(OtBu)-Trp(Boc)-Tag (**3ar**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (157.4 mg, 0.60 mmol), Fmoc-Asp(OtBu)-OH (123.4 mg, 0.30 mmol), and $\text{H}_2\text{N-Trp(Boc)-Tag}$ (208.7 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm 2) under Ar at room temperature. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Trp(Boc)-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 96% yield (275.8 mg) as white solid.

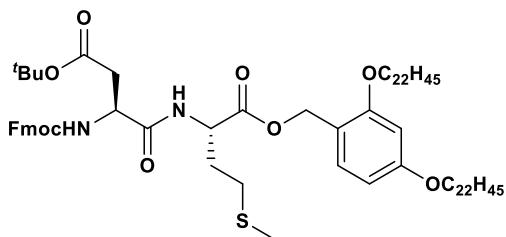
^1H NMR (CDCl_3 , 400 MHz) δ 8.10 (1H, d, $J = 6.4$ Hz), 7.75 (2H, d, $J = 7.3$ Hz), 7.60-7.43 (4H, m), 7.38 (2H, t, $J = 7.3$ Hz), 7.32-7.25 (3H, m), 7.24-7.12 (2H, m), 7.02 (1H, d, $J = 8.2$ Hz), 6.45-6.32 (2H, m), 5.91 (1H, d, $J = 8.2$ Hz), 5.11 (1H, d, $J = 11.9$ Hz), 5.06 (1H, d, $J = 11.9$ Hz), 4.95-4.85 (1H, m), 4.59-4.45 (1H, m), 4.44-4.24 (2H, m), 4.18 (1H, t, $J = 7.3$ Hz), 3.97-3.85 (4H, m), 3.23 (2H, d, $J = 5.5$ Hz), 2.88 (1H, dd, $J = 16.9$ Hz, 3.2 Hz), 2.58 (1H, dd, $J = 16.9$ Hz, 6.9 Hz),

1.80-1.70 (4H, m), 1.63 (9H, s), 1.49-1.21 (85H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.3, 171.1, 170.2, 160.9, 158.4, 155.9, 149.5, 143.9, 143.7, 141.3, 131.1, 130.5, 127.7, 127.1, 125.1, 124.5, 122.6, 120.0, 119.0, 115.7, 115.3, 114.8, 104.5, 99.7, 83.5, 81.8, 68.2, 68.1, 67.3, 63.1, 52.9, 51.0, 47.1, 37.5, 31.9, 30.0, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 28.2, 28.0, 27.3, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{90}\text{H}_{137}\text{N}_3\text{O}_{11}$ 1459.0145, found 1459.0162.



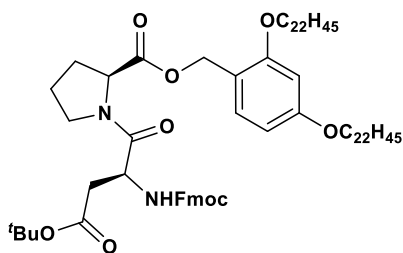
Fmoc-Asp(OtBu)-Cys(Trt)-Tag (**3as**). Following the general procedure, 2,6-lutidine (69.9 μL , 0.60 mmol), Bu_4NClO_4 (136.8 mg, 0.40 mmol), Ph_3P (157.4 mg, 0.60 mmol), Fmoc-Asp(OtBu)-OH (123.4 mg, 0.30 mmol), and $\text{H}_2\text{N-Cys(Trt)-Tag}$ (220.4 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 40 °C. After 4.8 F/mol of electricity based on $\text{H}_2\text{N-Cys(Trt)-Tag}$ was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 99% yield (297.8 mg) as white solid.

^1H NMR (CDCl_3 , 400 MHz) δ 7.75 (2H, d, $J = 7.8$ Hz), 7.57 (2H, t, $J = 7.8$ Hz), 7.42-7.25 (10H, m), 7.25-7.07 (11H, m), 6.43-6.34 (2H, m), 5.93 (1H, d, $J = 7.8$ Hz), 5.21-5.01 (2H, m), 4.60-4.50 (1H, m), 4.50-4.43 (1H, m), 4.42-4.29 (2H, m), 4.20 (1H, t, $J = 6.9$ Hz), 3.92 (2H, t, $J = 6.4$ Hz), 3.86 (2H, t, $J = 6.4$ Hz), 2.80 (1H, dd, $J = 17.4$ Hz, 3.7 Hz), 2.71-2.47 (3H, m), 1.81-1.63 (4H, m), 1.50-1.20 (85H, m), 0.88 (6H, t, $J = 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 171.0, 170.2, 169.8, 160.8, 158.3, 155.8, 144.3, 143.9, 143.7, 141.3, 141.3, 131.0, 129.5, 127.9, 127.7, 127.1, 126.8, 125.1, 120.0, 116.0, 104.6, 99.6, 81.8, 68.1, 68.1, 67.3, 66.8, 62.8, 51.7, 50.7, 47.1, 37.8, 33.7, 31.9, 29.7, 29.6, 29.4, 29.4, 29.3, 29.1, 28.0, 26.1, 26.0, 22.7, 14.1; HRMS (ESI-MS) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{96}\text{H}_{138}\text{N}_2\text{O}_9\text{S}$ 1518.0015, found 1518.0044.



Fmoc-Asp(O^tBu)-Met-Tag (**3at**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (123.4 mg, 0.30 mmol), and H₂N-Met-Tag (177.7 mg, 0.20 mmol) were added to Ar-purged MeCN(8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at 50 °C. After 4.8 F/mol of electricity based on H₂N-Met-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 99% yield (253.2 mg) as white solid.

¹H NMR (CDCl₃, 600 MHz) δ 7.76 (2H, d, J = 7.6 Hz), 7.64-7.51 (2H, m), 7.40 (2H, t, J = 7.6 Hz), 7.32 (2H, t, J = 7.6 Hz), 7.24-7.11 (2H, m), 6.45-6.35 (2H, m), 5.98 (1H, d, J = 8.3 Hz), 5.20 (1H, d, J = 11.7 Hz), 5.09 (1H, d, J = 11.7 Hz), 4.67 (1H, dd, J = 12.4 Hz, 7.6 Hz), 4.61-4.50 (1H, m), 4.41 (2H, d, J = 6.9 Hz), 4.23 (1H, t, J = 6.9 Hz), 3.96-3.85 (4H, m), 2.95 (1H, dd, J = 17.2 Hz, 3.4 Hz), 2.60 (1H, dd, J = 17.5 Hz, 6.2 Hz), 2.52-2.38 (2H, m), 2.20-2.09 (1H, m), 2.05-1.91 (4H, m), 1.81-1.70 (4H, m), 1.52-1.21 (85H, m), 0.88 (6H, t, J = 6.9 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 171.4, 171.4, 170.3, 161.0, 158.5, 156.0, 143.8, 143.7, 141.3, 131.4, 127.8, 127.1, 125.1, 120.0, 115.8, 104.5, 99.7, 82.0, 68.2, 68.1, 67.3, 63.1, 52.0, 51.0, 47.1, 37.5, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 28.0, 26.1, 26.0, 22.7, 15.3, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₇₉H₁₂₈N₂O₉S 1303.9233, found 1303.9235.



Fmoc-Pro-Asp(O^tBu)-Tag (**3au**). Following the general procedure, 2,6-lutidine (69.9 μ L, 0.60 mmol), Bu₄NClO₄ (136.8 mg, 0.40 mmol), Ph₃P (131.1 mg, 0.50 mmol), Fmoc-Asp(O^tBu)-OH (205.7 mg, 0.50 mmol), and H₂N-Pro-Tag (168.1 mg, 0.20 mmol) were added to Ar-purged MeCN (8.0 mL)-*c*-hex (4.0 mL). The solution was electrolyzed at constant current (0.67 mA/cm²) under Ar at room temperature. After 6.0 F/mol of electricity based on H₂N-Pro-Tag was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the product in 99% yield (249.5 mg) as white solid.

¹H NMR (CDCl₃, 400 MHz) δ 7.79-7.71 (2H, m), 7.62-7.51 (2H, m), 7.43-7.34 (2H, m), 7.34-7.26 (2H, m), 7.22-7.15 (0.83H, m, major rotamer), 7.15-7.08 (0.17H, m, minor rotamer), 6.46-6.33 (2H, m), 5.68 (0.83H, d, *J* = 8.9 Hz, major rotamer), 5.53 (0.17H, d, *J* = 9.2 Hz, minor rotamer), 5.21 (0.87H, d, *J* = 11.9 Hz, major rotamer), 5.15 (0.13H, d, *J* = 11.9 Hz, minor rotamer), 5.04 (0.87H, d, *J* = 11.9 Hz, major rotamer), 4.98 (0.13H, d, *J* = 11.9 Hz, minor rotamer), 4.94-4.85 (0.72H, m, major rotamer), 4.85-4.79 (0.12H, m, minor rotamer), 4.75-4.65 (0.13H, m, minor rotamer), 4.64-4.47 (1H, m), 4.44-4.25 (2H, m), 4.25-4.11 (1H, m), 3.98-3.83 (4H, m), 3.80-3.62 (2H, m), 2.77 (0.14H, dd, *J* = 16.0 Hz, 7.8 Hz, minor rotamer), 2.64 (0.86H, dd, *J* = 15.6 Hz, 4.6 Hz, major rotamer), 2.48 (1H, dd, *J* = 15.6 Hz, 8.2 Hz), 2.24-2.09 (1H, m), 2.08-1.92 (2H, m), 1.83-1.71 (4H, m), 1.49-1.21 (86H, m), 0.88 (6H, t, *J* = 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 171.6, 169.5, 169.5, 160.8, 158.3, 155.8, 143.8, 143.8, 141.3, 131.1, 127.7, 127.1, 125.2, 120.0, 116.3, 104.6, 99.7, 81.4, 68.1, 67.2, 62.5, 59.1, 49.8, 47.1, 46.9, 38.6, 31.9, 29.7, 29.6, 29.4, 29.4, 29.4, 29.3, 29.2, 29.0, 28.0, 26.1, 24.7, 22.7, 14.1; HRMS (ESI-MS) [M+Na]⁺ calcd for C₇₉H₁₂₆N₂O₉ 1269.9356, found 1296.9345.

2.5 Synthesis of Leuporelin

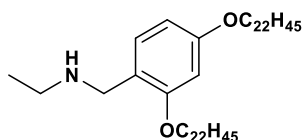
(1) Preparation of the Hydrophobic Benzyl Amine HCl salt

To a solution of the hydrophobic benzaldehyde (1.51 g, 2.0 mmol) in THF (45 mL)

ethylamine hydrochloride (815.4 mg, 10.0 mmol) and DMF (14 mL), DIPEA 3.4 mL, MgSO₄ (4.00 g), acetic acid (1.50 mL), and NaBH(OAc)₃ (211.9 mg x 4, 8.0 mmol) were added. The resulting reaction mixture was stirred at room temperature for 1.5 h followed by quench of remaining NaBH(OAc)₃ by 0.1 N HCl aq. The resulting reaction mixture was filtered and extracted with c-hex, and organic phase was washed with 0.1 HCl aq. and brine, dried over MgSO₄ and concentrated in vacuo. To a crude product, MeCN was added to give precipitants. The precipitants were collected by filtration and purified by column chromatography (CHCl₃: MeOH =50:1) to give the product as a white solid (1.29 g, 80% yield)

(2) Synthesis of Fmoc-Pro-NEtTag

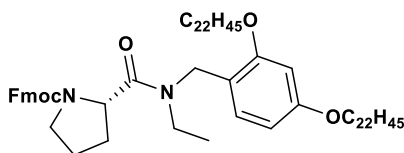
To a solution of hydrophobic benzyl amine (328.3 mg, 0.40 mmol) in THF (8.0 mL), Fmoc-Pro-OH·H₂O (202.4 mg, 0.60 mmol), DIPEA (224 μL, 1.32 mmol), and COMU (257.0 mg, 0.60 mmol) were added. The mixture was stirred for 20 min followed by solvent replacement with MeCN to give the product as a precipitate. Precipitate was collected by filtration and washed with MeCN to give the products quantitatively as light pink solid.



Hydrophobic benzyl amine

¹H NMR (CDCl₃, 600 MHz) δ 7.09 (1H, d, *J* = 7.6 Hz), 6.44-6.38 (2H, m), 3.96-3.91 (4H, m), 3.72 (2H, s), 2.62 (2H, q, *J* = 6.9 Hz), 1.82-1.73 (4H, m), 1.64 (1H, broad s), 1.49-1.22 (76H, m), 1.11 (3H, t, *J* = 6.9 Hz), 0.88 (6H, t, *J* = 6.9Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 159.5, 158.1,

130.4, 120.9, 104.2, 99.7, 68.1, 67.8, 49.0, 43.2, 31.9, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.3, 26.2, 26.1, 22.7, 15.3, 14.1.



Fmoc-Pro-NEtTag

^1H NMR (CDCl_3 , 600 MHz) δ 7.77-7.71 (2H, m), 7.68-7.50 (2H, m), 7.41-7.33 (2H, m), 7.33-7.23 (2H, m), 7.21-7.09 (0.8H, m), 6.89-6.84 (0.2H, m), 6.51-6.25 (1.8H, m), 5.91-5.87 (0.2H, m), 4.78-4.56 (2H, m), 4.49-4.23 (4H, m), 4.12-3.54 (7H, m), 3.51-3.17 (1H, m), 2.30-2.01 (2H, m), 1.99-1.83 (2H, m), 1.83-1.59 (4H, m), 1.47-1.21 (76H, m), 1.16-1.04 (3H, m), 0.88 (6H, t, J = 6.9 Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 172.5, 172.4, 172.3, 172.0, 159.8, 159.7, 159.5, 159.5, 157.9, 157.3, 157.1, 154.9, 154.9, 154.6, 154.4, 144.6, 144.5, 144.4, 144.3, 144.0, 143.9, 141.3, 141.3, 141.2, 141.2, 141.1, 130.5, 130.0, 127.9, 127.7, 127.6, 127.6, 127.4, 127.1, 127.1, 127.0, 127.0, 125.7, 125.4, 125.2, 125.1, 119.9, 119.8, 119.7, 118.1, 117.0, 116.5, 104.9, 104.7, 104.4, 104.0, 99.6, 99.4, 99.3, 68.1, 68.0, 68.0, 67.9, 67.7, 67.4, 67.3, 67.1, 66.7, 57.2, 57.1, 56.9, 56.6, 54.8, 47.4, 47.4, 47.4, 47.3, 47.3, 47.2, 47.0, 46.9, 45.0, 44.7, 42.3, 41.9, 41.6, 41.5, 41.4, 41.2, 38.4, 31.9, 31.4, 31.3, 30.3, 30.3, 29.7, 29.7, 29.6, 29.6, 29.4, 29.4, 29.3, 29.2, 26.2, 26.1, 26.0, 26.0, 24.5, 24.4, 23.4, 23.3, 22.7, 14.1, 14.1, 14.1, 14.0, 12.7, 12.6.

(3) General Procedure for Electrochemical Peptide Elongation*

MeCN (8.0 mL) and *c*-Hex (4.0 mL) were purged with Ar gas for 2 min. To a purged solvent, 2,6-lutidine (69.9 μL , 0.6 mmol), Bu_4NClO_4 (0.5 mmol), Ph_3P (157.4 mg, 0.6 mmol), Fmoc-protected amino acid (0.4 mmol), and *N*-deprotected tagged amino acid (0.2 mmol) were added. The solution was electrolyzed at constant current (0.67 mA/cm^2) under Ar at 40 $^\circ\text{C}$. After 4.8 F/mol of electricity based on *N*-deprotected tagged amino

acid was passed, the reaction mixture was extracted with *c*-hex (20 mL x 2), and then the solvent was replaced with MeCN. The resulting precipitants were collected by filtration and washed with MeCN to give the products.

* When condensation with (1) Fmoc-Arg(Pbf)-OH, (2) Fmoc-Ser(OtBu)-OH, and (3) pGlu, following conditions were applied.

(1) Fmoc-Arg(Pbf)-OH 3.5 eq., Ph₃P 5.0 eq., 6.0 F/mol, 60 °C.

(2) Fmoc-Ser(O^tBu)-OH 3.0 eq., Ph₃P 4.0 eq., 6.0 F/mol, 60 °C.

(3) pGlu 3.0 eq., Ph₃P 4.0 eq., 6.0 F/mol, 60 °C.

(4) Fmoc-deprotection of Peptides

Following the **2.3**, Fmoc was deprotected and products were obtained.

(5) Global deprotection of the protected leuprorelin (5)

To a solution of 2.5% triisopropylsilane and 2.5% H₂O in TFA, the protected form of leuprorelin (**5**) (20.0 mg, 0.0080 mmol) was added. The resulting reaction mixture was stirred at room temperature for 2h, followed by filtration using celite cake. Filtrate was concentrated in vacuo and DIPE (30 mL) was added. The resulting precipitate was recovered by cooling centrifugation and washed with DIPE (30 mL x 3). Lyophilization gave leuprorelin (**6**) quantitatively.

Leuprorelin (6)

White solid, HRMS (ESI-MS) [M+Na] calcd C₅₉H₈₄O₁₂N₁₆ for 1231.6347, found 1231.6350.

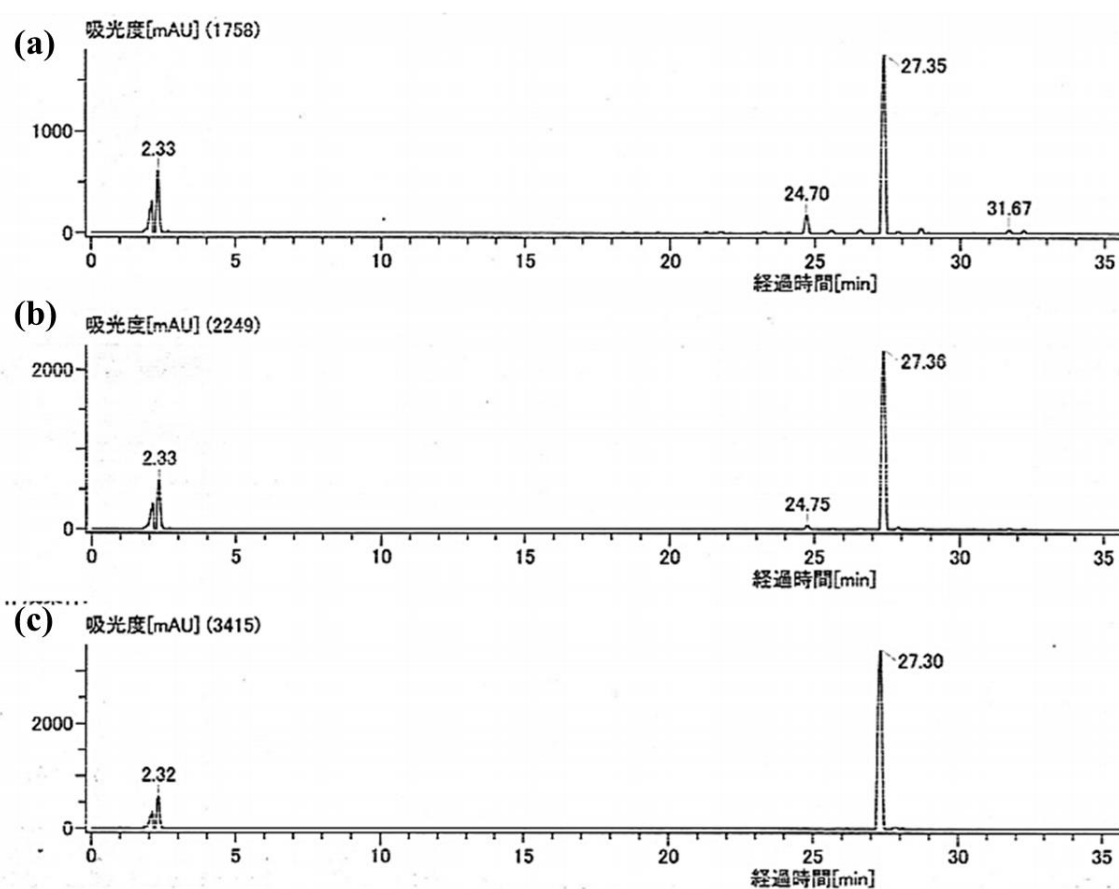


Figure S3. HPLC UV/Vis absorption spectrum (210-220 nm) of (a) synthesized, (b) synthesized and standard, and (c) standard sample of leuprorelin (**6**). C18 column was used a linear gradient of 15-42.5% acetonitrile in water, containing 0.1% trifluoroacetic acid.

3. ^1H and ^{13}C NMR Spectra of Compounds

